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CHEMOTHERAPY OF RODENT MALARIA

ANNUAL REPORT

PART TWO

WALLACE PETERS MD DSc

OCTOBER 1987

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MAY 06 1988
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Supported by
US ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701-5012

Contract No DAMD17-85-C-5172

Department of Medical Protozoology
London School of Hygiene and Tropical Medicine
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SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
1a. REPORT SECURITY CLASSIFICATION Unclassified			1b. RESTRICTIVE MARKINGS		
2a. SECURITY CLASSIFICATION AUTHORITY			3. DISTRIBUTION/AVAILABILITY OF REPORT Distribution limited to US Government Agencies only; Proprietary Information, April 21, 1988		
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE			5. MONITORING ORGANIZATION REPORT NUMBER(S)		
4. PERFORMING ORGANIZATION REPORT NUMBER(S)					
6a. NAME OF PERFORMING ORGANIZATION London School of Hygiene and Tropical Medicine		6b. OFFICE SYMBOL (If applicable)		7a. NAME OF MONITORING ORGANIZATION	
6c. ADDRESS (City, State, and ZIP Code) Keppel Street, WEIE 7HT London				7b. ADDRESS (City, State, and ZIP Code)	
8a. NAME OF FUNDING/SPONSORING ORGANIZATION U.S. Army Medical Research & Development Command		8b. OFFICE SYMBOL (If applicable) SGRD-RMI-S		9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER Contract No. DAMD17-85-C-5172	
8c. ADDRESS (City, State, and ZIP Code) Fort Detrick Frederick, Maryland 21701-5012		10. SOURCE OF FUNDING NUMBERS			
		PROGRAM ELEMENT NO. 62770A		PROJECT NO. 3MI-62770A870	TASK NO. AJ
				WORK UNIT 010	ACCESSION NO.
11. TITLE (Include Security Classification) Chemotherapy of Rodent Malaria					
12. PERSONAL AUTHOR(S) Peters, Wallace, M.D., DSc.					
13a. TYPE OF REPORT Annual Report, Part Two		13b. TIME COVERED FROM 7/1/86 TO 6/30/87		14. DATE OF REPORT (Year, Month, Day) 1987 October	
15. PAGE COUNT					
16. SUPPLEMENTARY NOTATION Annual Report consists of Parts One and Two					
17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)		
FIELD	GROUP	SUB-GROUP			
06	13		Chemotherapy, Infectious Diseases, Malaria, Mice		
06	15				
19. ABSTRACT (Continue on reverse if necessary and identify by block number)					
20. DISTRIBUTION/AVAILABILITY OF ABSTRACT <input type="checkbox"/> UNCLASSIFIED/UNLIMITED <input checked="" type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS			21. ABSTRACT SECURITY CLASSIFICATION Unclassified		
22a. NAME OF RESPONSIBLE INDIVIDUAL Mrs. Virginia M. Miller			22b. TELEPHONE (Include Area Code) 301/663-7325		22c. OFFICE SYMBOL SGRD-RMI-S

DD Form 1473, JUN 86

Previous editions are obsolete.

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FOREWORD

In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

1. INTRODUCTION

Until September 1987, no new compounds had been submitted during this second year of the contract. As a result of this, the main emphasis of the work has been on our continuing studies into drug resistance, involving further examinations of cross-resistance patterns in resistant lines. In addition, ultrastructural studies comparing treated and untreated parasites resistant to a wide range of antimalarials have been carried out. Some preliminary studies into the in vivo effect of calcium channel blockers on chloroquine resistant strains of rodent malaria have also been undertaken.

A problem which was encountered with a virus infection in our mosquito colony stimulated a series of studies into the action of some antiviral agents on polyhedrosis virus in Anopheles stephensi. Ultrastructural studies of treated and control mosquitoes are included in this report. *Keywords: chemotherapy*

In response to a request from Dr T Sweeney, definitive test data from all blood schizontocidal and causal prophylactic tests were assembled. Where necessary the test results were recalculated using our current procedures in order to provide data which could be validly compared. These data are appended to the Report as Appendices 5.3 and 5.4.

2. ADMINISTRATIVE EVENTS

Staff employed on US Army funds are as follows:

Senior Technologist/ Research Assistant	- Mr B L Robinson	100% Time
Technicians	- Ms A West	100% Time
	- Ms J R Cox	100% Time
Secretary	- Mrs B A Sargeant	25% Time

Other staff associated with the project but not financially

APPENDICES

APPENDIX 1

UPDATED SUMMARY OF RESISTANCE FACTORS (I90)
OBTAINED IN CROSS-RESISTANCE STUDIES

"Original contains color
plates: All DTIC reproductions
will be in black and
white"



Accession For	
NTIS GRA&I	<input type="checkbox"/>
DTIC TAB	<input checked="" type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
B-3	

	N	RC	Q	NI100	NH	P	B	PYR	ORA	MEN	NPN	NI708	MEY	KFY	PFMA	NI765	NAM	QM
CHLOROQUINE	3.1	230	>60	4.5	7.0	2.3	4.8	3.5	3.6	3.0	25.0	10.2				4.0		305
AMODIAQUINE	2.6	420	>30	20.0	5.4	2.0	2.1	3.3	2.6	4.5	32.0	5.2	6.2	2.6				300
WR 228258	10.0	13.0	>100	26.0	>100	<3.0	<3.0	<3.0	<3.0	<3.0	141	178	1.3	<3.0	<3.0	97.7	3400	>100
PRIMAQUINE	4.8	13.0	18.5	9.0	10.5	74.0	6.4	24.0	2.6	3.3	8.4	7.0				9.2		21.0
QUININE	118	1280	>600	1700	210	140	170	130	190	40.0	900	175				310		2000
CINCHONINE	125	4700	>600	400	290	85.0	50.0	91.0	63.0	60.0	550	90.0	257	25.4		275		>600
QUINIDINE	31.0	92.0	470	305	117	85.0	35.0	93.0	54.0		580	88.0	152	71.0	127	100	550	700
MEFLOQUINE	4.6	275	>60	540	9.0	13.5	6.0	5.6	4.2	2.5	6.8	5.3				4.4		850
HALOFANTRINE	1.1	>100	>100	135	3.6	1.5	4.2	2.3	1.9	0.7	3.5	1.5	2.0	3.4	2.3	1.1	30.0	>100
MEPACRINE	1.9	17.0	>30	195	4.7	2.9	4.6	1.1	2.1		45.0	12.3	4.8	3.4	16.0	38.0	>10	>30
ARTEMISININ	4.2	430	267	17.0	10.5	12.0	8.2	4.8	7.5	6.2	90.0	5.9	9.5	8.8	20.8	13.9	538	52.0
PYRONARIDINE	0.7	10.0	>100	1.6	0.8	1.0	1.4	1.1	1.5	0.7	13.5	0.7	0.9	0.7		1.3		
PRIMETHAMINE	0.12	0.05	0.03	0.04	0.26	0.17	2.4	3.4	0.5	0.4	0.21	0.01	29.6	3.7	0.07		0.26	0.05
SULFADOXINE	4.4	0.62	0.13	0.04	2.7	0.39	0.71	1.2	29.0	0.34	0.1	1.2				0.9		0.12
FANSIDAR *	0.32	0.06	0.01	0.03	0.16	0.2	0.5	0.6	0.48	0.07	0.03	0.1				0.33		0.05
CYCLOQUINIL	3.3	3.6	3.4	2.5	0.4	320	>100	>100	44.0	5.2	10.0	3.7				3.5		4.0
MENOCITONE	1.4	11.0	1.8	1.2	1.6	2.1	9.0	7.2	2.7	>30	1.8	2.3				1.5		
FLOXACRINE	1.0	0.27	0.5	0.3	0.8	0.4	0.4	0.4	0.4	1.0	0.3	0.6			0.4	0.8	0.7	0.7
CLINDAMYCIN	36.0	56.0	9.7	2.9	57.0	6.4	27.0	6.0	8.8	7.5	9.0	27.0				19.0		
DOXYCYCLINE	2.7	3.8	9.3	33.0	20.0	3.2	17.5	8.5	180	13.0	9.0	>10	>10	5.1	42.0	12.0	11.5	18.0
LOX 1765	1.7	8.2	560	34.5	39.0	2.1	3.1	3.2	4.0	5.1	6.6	11.0		4.8		100		

* Pyrimethamine : Sulfadoxine (1:3)

Table 1. ED₉₀ values of some antimalarial drugs against resistant lines of P. berghei.

	N	RC	Q	N100	NH	P	B	PYR	ORA	MEN	NPN	N1708	MFY	KFY	PFMA	N1765	NAM	QM
CHLOROQUINE	1.0	74.2	>19.4	1.5	2.3	0.7	1.5	1.1	1.2	1.0	8.1	3.3				1.3		98.4
AMODIAQUINE	1.0	162	11.5	7.7	2.1	0.8	0.8	1.3	1.0	1.7	12.3	2.0	2.4	1.0				115
WR 228258	1.0	1.3	>10	2.6	>10	<0.3	<0.3	<0.3	<0.3	<0.3	14.1	17.8	0.13	<0.3	<0.3	9.8	340	>10
PRIMAQUINE	1.0	2.7	3.9	1.9	2.2	15.4	1.3	5.0	0.5	0.7	1.8	1.5				1.9		4.4
QUININE	1.0	10.8	>5.0	14.4	1.8	1.2	1.4	1.1	1.6	0.3	7.6	1.5				2.6		16.9
CINCHONINE	1.0	37.6	>4.8	3.2	2.3	0.7	0.4	0.7	0.5	0.5	4.4	0.7	2.1	0.2		2.2		>4.8
QUINIDINE	1.0	3.0	15.2	9.8	3.8	2.7	1.1	3.0	1.7		18.7	2.8	4.9	2.3	4.1	3.2	17.7	22.6
MEFLOQUINE	1.0	60.0	>13	117	2.0	2.9	1.3	1.2	0.9	0.5	1.5	1.2				1.0		185
HALOFANTRINE	1.0	>91	>91	123	3.3	1.4	3.8	2.1	1.7	0.6	3.2	1.4	1.8	3.1	2.1	1.0	27.3	>91
MEPRACRINE	1.0	8.9	>15.8	103	2.5	1.5	2.4	0.6	1.1		23.7	6.5	2.5	1.8	3.4	20.0	>5.3	>15.8
ARTEMISININ	1.0	102	63.5	4.0	2.5	2.9	2.0	1.1	1.8	1.5	21.4	1.4	2.3	2.1	5.0	3.3	128	12.4
PRONARIDINE	1.0	14.3	>143	2.3	1.1	1.4	2.0	1.6	2.1	1.0	19.3	1.0	1.3	1.0		1.9		
PYRIMETHAMINE	1.0	0.4	0.25	0.3	2.2	1.4	20.0	28.3	4.2	3.3	1.8	0.08	247	30.8			2.2	0.4
SULFADOXINE	1.0	0.14	0.03	0.01	0.6	0.09	0.16	0.3	6.6	0.08	0.02	0.3				0.2		0.03
FANSIDAR	1.0	0.18	0.03	0.25	0.5	0.6	1.6	1.9	1.5	0.2	0.09	0.3				1.0		0.16
CYCLOQUANIL	1.0	1.1	1.0	0.8	1.9	97.0	>30	>30	13.3	1.6	3.0	1.1				1.1		1.2
MENOCTONE	1.0	7.9	1.3	0.9	1.1	1.5	6.4	5.1	1.9	>21	1.3	1.6				1.1		
FLOXACRINE	1.0	0.3	0.5	0.3	0.8	0.4	0.4	0.4	0.4	1.0	0.3	0.6			0.4	0.8	0.7	0.7
CLINDAMYCIN	1.0	1.6	0.3	0.1	1.6	0.2	0.8	0.2	0.2	0.2	0.3	0.8				0.5		
DOXYCYCLINE	1.0	1.4	3.4	12.2	7.4	1.2	6.5	3.1	66.7	4.8	3.3	>37	>3.7	1.9	15.6	4.4	4.3	6.7
LON 1765	1.0	4.8	329	20.3	22.9	1.2	1.8	1.9	2.4	3.0	3.9	6.5		2.8		58.8		

>5.0 Resistant 25-50 Slightly resistant 0.7-2.5 Sensitive 0.5-0.7 Slightly hypersensitive <0.5 Hypersensitive

Table 2. Resistance factors (I_{90}) of resistant strains of *P. berghei* to some antimalarial drugs.

	NS	NS1100	SH	SPN	NS1708	ART	NS1765	SAM	MPS	Qms	NIG
CHLOROQUINE	56.0	27.0	80.0	220	21.5	400	210				6.7
AMODIAQUINE	18.0	4.8	»100	420	31.0	310	78.3				6.3
WR 228258	2.9	90.0	0.4	156	125	»30	140	>100	»100	145	<3.0
PRIMAQUINE	8.4	18.4	9.2	13.7	9.0	11.5	10.2				19.5
QUININE	290	600	190	920	200	400	270				220
CINCHONINE	220	70.0	»600	1600	155	700	253				115
QUINIDINE	195	230	1050	1000	72.0	385	115	490	620	5400	115
MEFLOQUINE	7.2	640	»100	20.0	7.5	65.0	11.0				5.2
HALOFANTRINE	1.0	22.5	375	3.4	0.9	6.5	5.7	60.0	»30	»30	2.0
MEPRARINE	18.3	120	78.0	>30	11.8	250	23.5	>30	>10	»10	13.0
ARTEMISININ	10.0	13.8	»30	20.5	7.8	165	6.5	22.5	200	120	11.5
PYRONARIDINE	1.2	1.4	>100	33.5	1.4	19.5	2.2	3.2	14.3	46.0	0.7
PYRIMETHAMINE		0.08				0.05					
SULFADOXINE	0.26	0.08	0.21	0.08	0.14	0.05	0.13				0.18
FANSIDAR	0.1	0.14	0.19	0.08	0.1	0.05	0.1				0.04
CYCLOQUANIL	6.9	4.8	6.8	11.5	5.0	6.3	2.4				12.3
MENOCTONE	4.5	3.1	3.8	4.3	3.5	1.2	3.0				
FLOXALRINE	0.6	0.5	0.5	0.6	0.4	0.3					0.3
CLINDAMYUN	55.0	18.5	14.0	24.0	24.0	10.0	14.0				
DOXYCYCLINE	>10	28.0	17.0	>10	34.0	32.0	15.5	58.0	42.0	13.8	>10
LON 1765	6.0	8.2	18.0	56.0	11.2	125	220	10.6	18.0	70.0	5.4

Table 3. ED_{90} values of some antimalarial drugs against resistant lines of P. yoelii ssp. and P. y. nigeriensis (NIG).

	NS	NS1100	SH	SPN	NS1708	ART	NS1765	SAM	MPS	QMS	NIG
CHLOROQUINE	1.0	0.5	1.4	3.9	0.4	7.1	3.8				0.1
AMODIAQUINE	1.0	0.3	>5.6	23.3	1.7	17.2	4.4				0.4
WR 228258	1.0	31.0	0.1	53.8	43.1	>10.3	48.3	>34.5	>34.5	50.0	<1.0
PRIMAQUINE	1.0	2.2	1.1	1.6	1.1	1.4	1.2				2.3
QUININE	1.0	2.1	0.7	3.2	0.7	1.4	0.9				0.8
CINCHONINE	1.0	0.3	>2.7	7.3	0.7	3.2	1.2				0.5
QUINIDINE	1.0	1.2	5.4	5.1	0.4	2.0	0.6	2.5	3.2	27.7	0.6
MEFLOQUINE	1.0	88.9	>13.9	2.8	1.0	9.0	1.5				0.7
HALOFANTHINE	1.0	22.5	375	3.4	0.9	6.5	5.7	60.0	>30	>30	2.0
MEPACRINE	1.0	6.6	4.3	>1.6	0.6	13.7	1.3	>1.6	>0.5	>0.5	0.7
ARTEMISININ	1.0	1.4	>3.0	2.1	0.8	16.5	0.7	2.3	20.0	12.0	1.2
PYRONARIDINE	1.0	1.2	>83.3	27.9	1.2	16.3	1.8	2.7	11.9	38.3	0.6
PYRIMETHAMINE											
SULFADOXINE	1.0	0.3	0.8	0.3	0.5	0.2	0.5				0.7
FANSIDAR	1.0	1.4	1.9	0.8	1.0	0.5	1.0				0.4
CYCLOQUANIL	1.0	0.7	1.0	1.7	0.7	0.9	0.3				1.8
MENOCTONE	1.0	0.7	0.8	1.0	0.8	0.3	0.7				
FLOXALURINE	1.0	0.8	0.8	1.0	0.7	0.5					0.5
CLINDAMYCIN	1.0	0.3	0.3	0.4	0.4	0.2	0.3				
DOXYCYCLINE	1.0	<2.8	<1.7	1.0	<3.4	<3.2	<1.6	<5.8	<4.2	<1.4	1.0
LON 1765	1.0	1.4	3.0	9.3	1.9	20.8	36.7	1.8	3.0	11.7	0.9

Table 4. I_{90} values of resistant strains of P. yoelii ssp. and P. y. nigeriensis (NIG) to some antimalarial drugs.

APPENDIX 2

SUMMARY OF DATA OBTAINED FROM "4-DAY" BLOOD SCHIZONTICIDAL
TESTS IN CROSS-RESISTANCE STUDY.

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 5

COMPOUND NAME

OR NUMBER

Chloroquine

PARASITE (SUB)SPECIES *P. berghei*

FORMULATION

Tween 80/H₂O

ROUTE OF ADMINISTRATION : SC/HP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated Control
	3.0	5		-	97.2 ± 1.2
	10.0	5		-	70.3 ± 3.5
QM	30.0	5	1	-	66.4 ± 3.2
	100.0	5		-	61.3 ± 5.2
	∅	10			
ED ₅₀ (range) 55.0(15.0 - 160)					
ED ₉₀ (range) 305(85.0 - 925)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 6

COMPOUND NAME

OR NUMBER Chloroquine PARASITE (SUB)SPECIES P. yoelii

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) ~100.. MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x100
	10.0	5		-	92.2 ± 6.0
	30.0	5		-	76.4 ± 7.4
QS	60.0	5	1	-	60.7 ± 17.3
	100.0	5		-	37.2 ± 15.8
	∅	10		18.0	
ED ₅₀ (range) <u>70.0(32.0 - 170)</u>					
ED ₉₀ (range) <u>400(185 - 960)</u>					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 7

COMPOUND NAME

OR NUMBER .AMODIAQUINE..... PARASITE (SUB)SPECIES *P. berghei*....

FORMULATION .Tween 80./H₂O. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	3.0	5		-	100 ± 5.7
	10.0	5		-	87.8 ± 5.7
QM	30.0	5	1	-	59.8 ± 5.5
	100.0	5		-	53.8 ± 10.2
	Ø	10		8.7	

ED₅₀(range) 64.0(33.0 - 145)

ED₉₀(range) 300(155 - 700)

Resistance factor I₉₀

ED₅₀(range)

ED₉₀(range)

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 8

COMPOUND NAME

OR NUMBER AMODIAQUINE PARASITE (SUB)SPECIES P. yoelii ssp.

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	3.0	5		-	67.1 ± 8.3
	10.0	5		-	52.2 ± 8.0
QS	30.0	5	1	-	38.3 ± 8.8
	100.0	5		-	20.0 ± 7.3
	Ø	10		19.8	
ED ₅₀ (range) 10.5 (4.8 - 24.0)					
ED ₉₀ (range) 310 (140 - 680)					
Resistance factor I ₉₀ 119.2					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIOES)

TABLE 9

COMPOUND NAME WR 228258

OR NUMBER ... LON. 1708 PARASITE (SUB)SPECIES *P. berghei*

FORMULATION *Tween 80/H₂O* ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	3.0	5		-	93.5 ± 7.0
	10.0	5		-	96.5 ± 4.3
Q	30.0	5	1	-	100 ± 1.9
	100.0	5		-	93.0 ± 4.6
	∅	10		8.0	
ED ₅₀ (range) > 100					
ED ₉₀ (range) » 100					
Resistance factor I ₉₀					
	3.0	5		-	89.7 ± 10.5
	10.0	5		-	85.8 ± 12.4
NH	30.0	5	1	-	71.0 ± 6.8
	100.0	5		-	64.1 ± 9.7
	∅	10		9.3	
EO ₅₀ (range) > 100					
EO ₉₀ (range) » 100					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 10

COMPOUND NAME WR 228258

OR NUMBER ... LON 1708 ... PARASITE (SUB)SPECIES *P. berghei* ...

FORMULATION *Tween 80 / H₂O*. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	3.0	5		-	0
	10.0	5		-	0
P	30.0	5	1	-	0
	100.0	5		-	0
	Ø	10		17.4	
ED ₅₀ (range) < 3.0					
ED ₉₀ (range) < 3.0					
Resistance factor I ₉₀					
	3.0	5		-	0.5 ± 0.3
	10.0	5		-	0
B	30.0	5	1	-	0
	100.0	5		-	0
	Ø	10		20.8	
ED ₅₀ (range) < 3.0					
ED ₉₀ (range) < 3.0					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 11

COMPOUND NAME **WR 228258**

OR NUMBER **....LON.1702.....** PARASITE (SUB)SPECIES **P. berghei....**

FORMULATION **Tween 80/H₂O.** ROUTE OF ADMINISTRATION : **SC/IT/PO/IV**

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	3.0	5		-	0.4 ± 0.4
	10.0	5		-	0
PYR	30.0	5	1	-	0
	100.0	5		-	0
	Ø	10		15.7	
ED ₅₀ (range) < 3.0					
ED ₉₀ (range) < 3.0					
Resistance factor I ₉₀					
	3.0	5		-	0.02 ± 0.02
	10.0	5		-	0
ORA	30.0	5	1	-	0
	100.0	5		-	0
	Ø	10		12.7	
ED ₅₀ (range) < 3.0					
ED ₉₀ (range) < 3.0					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 12

COMPOUND NAME **WR 228258**

OR NUMBER **... LON. 1708** PARASITE (SUB)SPECIES **P. berghei**....

FORMULATION **Tween 80 / H₂O** ROUTE OF ADMINISTRATION : **SC / IP / PO / IV**

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	3.0	5		-	0.2 ± 0.08
	10.0	5		-	0
MEN	30.0	5	1	-	0
	100.0	5		-	0
	∅	10		23.5	
ED ₅₀ (range) < 3.0					
ED ₉₀ (range) < 3.0					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 13

COMPOUND NAME **WR 228258**

OR NUMBER **LON 1708**..... PARASITE (SUB)SPECIES **P. berghei**.....

FORMULATION **Trim 80/H₂O** ROUTE OF ADMINISTRATION : SC/~~IP~~/~~PO~~/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x100
	3.0	5		-	75.2 ± 3.4
	10.0	5		-	56.3 ± 4.2
NPN	30.0	5	1	-	51.1 ± 5.2
	100.0	5		-	49.0 ± 0.3
	Ø	10		19.4	

ED₅₀(range) **30.0 (11.0 - 95.0)**

ED₉₀(range) **> 100**

Resistance factor I₉₀

	3.0	5		-	0.01 ± 0.01
	10.0	5		-	0
PFMA	30.0	5	1	-	0
	100.0	5		-	0
	Ø	10		14.6	

ED₅₀(range) **< 3.0**

ED₉₀(range) **< 3.0**

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 14

COMPOUND NAME WR 228258

OR NUMBER LON 1798 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION : SC/TP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	3.0	5		-	69.8 ± 7.1
	10.0	5		-	81.2 ± 5.1
NAM	30.0	5	1	-	68.4 ± 5.3
	100.0	5		-	52.8 ± 6.6
	Ø	10		11.6	

ED₅₀(range) 110(67.0 - 175)

ED₉₀(range) 3400(2100 - 5200)

Resistance factor I₉₀

	3.0	5		-	100 ± 3.5
	10.0	5		-	85.5 ± 10.3
QM	30.0	5	1	-	80.5 ± 10.3
	100.0	5		-	72.3 ± 5.9
	Ø	10		8.8	

ED₅₀(range) > 100

ED₉₀(range) > 100

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 15

COMPOUND NAME **WR 228258**

OR NUMBER **LON 1708** PARASITE (SUB)SPECIES **P. berghei**

FORMULATION **Tween 80/H₂O** ROUTE OF ADMINISTRATION : **SC/ID/PO/IV**

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	3.0	5		-	61.8 ± 13.7
	10.0	5		-	38.3 ± 19.2
NS 1100	30.0	5	1	-	22.9 ± 14.1
	100.0	5		-	16.1 ± 6.2
	Ø	10		5.6	

ED₅₀(range) **7.5(1.8 - 22.5)**

ED₉₀(range) **90.0(21.0 - 260)**

Resistance factor I₉₀

	3.0	5		-	63.1 ± 4.0
	10.0	5		-	54.1 ± 5.5
SAM	30.0	5	1	-	46.6 ± 4.6
	100.0	5		-	36.8 ± 4.5
	Ø	10		22.2	

ED₅₀(range) **15.5(7.5 - 34.0)**

ED₉₀(range) **> 100**

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 16

COMPOUND NAME **WR 228258**

OR NUMBER **LON 1708** PARASITE (SUB)SPECIES **P. yoelii**

FORMULATION **Tween 80/H₂O**. ROUTE OF ADMINISTRATION : **SC/IP/IPQ/IV**

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x/100}
	1.0	5		-	100 ± 3.3
	3.0	5		-	89.6 ± 7.9
QS	10.0	5	1	-	78.9 ± 5.2
	30.0	5		-	78.0 ± 11.4
	∅	10		18.0	
ED ₅₀ (range) > 30					
ED ₉₀ (range) >> 30					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 17

COMPOUND NAME **WR 228258**
OR NUMBER **LON 1708** PARASITE (SUB)SPECIES **P. berghei**
FORMULATION **Twon 80/H₂O** ROUTE OF ADMINISTRATION : **SC/IP/PO/IV**
MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	3.0	5		-	100 ± 3.0
	10.0	5		-	86.6 ± 9.6
QMS	30.0	5	1	-	100 ± 1.7
	100.0	5		-	45.9 ± 8.6
	∅	10		5.8	
ED ₅₀ (range) 96.0(85.0 - 105)					
ED ₉₀ (range) 145(130 - 160)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 18

COMPOUND NAME

OR NUMBER

PRIMAQUINE

PARASITE (SUB)SPECIES *P. berghei*

FORMULATION

Tween 80/H₂O

ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	3.0	5		-	76.1 ± 10.2
	10.0	5		-	64.4 ± 14.1
QM	30.0	5	1	-	2.3 ± 1.3
	60.0	5		-	0
	∅	10		8.7	
ED ₅₀ (range) 7.6(4.0 - 18.5)					
ED ₉₀ (range) 21.0(11.0 - 51.0)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 19

COMPOUND NAME

OR NUMBER ..PRIMAQUINE..... PARASITE (SUB)SPECIES *P. yoelii* sp.

FORMULATION *Tween 80/H₂O*. ROUTE OF ADMINISTRATION : SC/~~IP~~/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ¹⁰⁰
	1.0	5		-	57.3 ± 6.0
	3.0	5		-	44.7 ± 6.8
QS	10.0	5	1	-	39.3 ± 8.9
	30.0	5		-	1.9 ± 1.7
	∅	10		19.8	
ED ₅₀ (range) 2.7(1.1 - 9.5)					
ED ₉₀ (range) 11.5(4.7 - 40.0)					
Resistance factor I ₉₀ 1.3					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 20

COMPOUND NAME

OR NUMBER Quinine hydrochloride PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/HP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	30.0	5		-	89.7 ± 11.5
	100.0	5		-	58.3 ± 8.6
RC	300.0	5	1	-	45.8 ± 22.6
	600.0	5		-	25.8 ± 6.9
	∅	10		6.0	
ED ₅₀ (range) 180(95.0-600)					
ED ₉₀ (range) 1280(680-4300)					
Resistance factor I ₉₀ 10.8					
	30.0	5		-	100 ± 5.5
	100.0	5		-	45.6 ± 9.5
ORA	300.0	5	1	-	1.6 ± 0.7
	600.0	5		-	0.3 ± 0.2
	∅	10		14.1	
ED ₅₀ (range) 80(58 - 110)					
ED ₉₀ (range) 190(140 - 260)					
Resistance factor I ₉₀ 1.6					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 21

COMPOUND NAME

OR NUMBER QUININE HYDROCHLORIDE PARASITE (SUB)SPECIES P. berghei....

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X 100
	30.0	5		-	98.6 ± 7.9
	100.0	5		-	66.7 ± 10.2
QM	300.0	5	1	-	63.2 ± 17.7
	600.0	5		-	54.0 ± 8.4
	Ø	10		8.7	

ED₅₀(range) 410 (120 - 850)

ED₉₀(range) 2000 (570 - 4000)

Resistance factor I₉₀

ED₅₀(range)

ED₉₀(range)

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 22

COMPOUND NAME

OR NUMBER ..QUININE HYDROCHLORIDE.. PARASITE (SUB)SPECIES *P. yoelii* ssp..

FORMULATION *Tween 80/H₂O*.. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	30.0	5		-	73.5 ± 23.1
	100.0	5		-	49.8 ± 16.4
QS	300.0	5	1	-	41.3 ± 2.0
	600.0	5		-	5.3 ± 5.3
	Ø	10		19.8	
ED ₅₀ (range) 100(30.0 - 250)					
ED ₉₀ (range) 400(120 - 1000)					
Resistance factor I ₉₀ 3.4					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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TABLE 23

OR NUMBER

Quinine hydrochloride.

PARASITE (SUB)SPECIES

P. yoelii

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION : SC/IV/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	30.0	5		-	100 ± 4.2
	100.0	5		-	50.2 ± 29.9
NIG	300.0	5	1	-	3.9 ± 2.9
	600.0	5		-	0.1 ± 0.1
	Ø	10		26.7	

$EO_{50}(\text{range}) 87.5(53.0 - 180)$

ED₉₀(range) 220(135 - 460)

Resistance factor I_{90} 1.9

[illegible]

EO₅₀(range)

EO₉₀(range)

Resistance factor I_{90}

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 24

COMPOUND NAME

OR NUMBER *Cinchonine hydrochloride* PARASITE (SUB)SPECIES *P. berghei*

FORMULATION *Tween 80/H₂O*... ROUTE OF ADMINISTRATION : *SC/IV/PO/IV*

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	30.0	5		-	77.5 ± 9.9
	100.0	5		-	80.4 ± 9.9
RC	300.0	5	1	-	68.8 ± 12.2
	600.0	5		-	42.5 ± 6.6
	∅	10		6.0	

ED₅₀(range) 510(260 - 1300)

ED₉₀(range) 4700(2300 - 11500)

Resistance factor I₉₀ 37.6

	30.0	5		-	31.2 ± 9.7
	100.0	5		-	11.8 ± 3.6
ORA	300.0	5	1	-	0
	600.0	5		-	0
	∅	10		14.1	

ED₅₀(range) 28.5(17.5 - 52.0)

ED₉₀(range) 63.0(39.0 - 115)

Resistance factor I₉₀ 0.5

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 25

COMPOUND NAME

OR NUMBER CINCHONINE HYDROCHLORIDE PARASITE (SUB)SPECIES *P. berghei*.....

FORMULATION *Tween 80/H₂O*... ROUTE OF ADMINISTRATION : *SC/IP/PO/IV*

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	30.0	5		-	86.2 ± 12.8
	100.0	5		-	70.6 ± 13.7
QM	300.0	5	1	-	65.3 ± 17.4
	600.0	5		-	60.5 ± 19.0
	∅	10		8.7	

ED₅₀(range) *750(175 - 8000)*

ED₉₀(range) *>> 600*

Resistance factor I₉₀

ED₅₀(range)

ED₉₀(range)

Resistance factor I₉₀

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 26

COMPOUND NAME

OR NUMBER ... CINCHONINE HYDROCHLORIDE PARASITE (SUB)SPECIES *P. yoelii* ssp.

FORMULATION ... Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	30.0	5		-	98.4 ± 4.8
	100.0	5		-	73.5 ± 4.1
QS	300.0	5	1	-	47.1 ± 14.0
	600.0	5		-	> LD ₁₀₀
	∅	10		19.8	
ED ₅₀ (range) 220(150 - 400)					
ED ₉₀ (range) 700(500 - 1250)					
Resistance factor I ₉₀ 5.6					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 27

COMPOUND NAME

OR NUMBER Cinchonine hydrochloride PARASITE (SUB)SPECIES P. yoelii.....

FORMULATION Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC/IT/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	30.0	5		-	83.7 ± 4.0
	100.0	5		-	49.9 ± 15.6
NIG	300.0	5	1	-	0.4 ± 0.3
	600.0	5		-	0
	∅	10		26.7	
ED ₅₀ (range) 74.0(41.0-125)					
ED ₉₀ (range) 115(90.0-280)					
Resistance factor I ₉₀ 0.9					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIOES)

TABLE 28

COMPOUND NAME

OR NUMBER .QUINIDINE HYDROCHLORIDE. PARASITE (SUB)SPECIES ...*P. berghei*....

FORMULATION ..Tween 80/H₂O.. ROUTE OF ADMINISTRATION : ~~SC/IV~~/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	10.0	5		-	43.6 ± 12.7
	30.0	5		-	12.6 ± 4.3
N	60.0	5	1	-	4.9 ± 1.8
	100.0	5		-	0.3 ± 0.3
	300.0	5		-	0
	∅	10		9.4	
E ₀ ₅₀ (range) 10.0(3.7-16.5)					
E ₀ ₉₀ (range) 31.0(11.0-50.0)					
Resistance factor I ₉₀ 1.0					
	60.0	5		-	100 ± 24.3
	100.0	5		-	2.5 ± 1.7
RC	300.0	5	1	-	0
	∅	10		3.3	
E ₀ ₅₀ (range) 82.0(74.0-91.0)					
E ₀ ₉₀ (range) 92.0(82.0-102)					
Resistance factor I ₉₀ 3.0					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 29

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/IV/PO/IT

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X 100
	60.0	5		-	100 ± 12.6
	100.0	5		-	62.8 ± 13.2
N 1100	300.0	5	1	-	13.2 ± 6.0
	600.0	5		-	11.2 ± 7.5
	Ø	10		2.9	
ED ₅₀ (range) 200 (98.0 - 430)					
ED ₉₀ (range) 305 (150 - 660)					
Resistance factor I ₉₀ 9.8					
	60.0	5		-	100 ± 10.1
	100.0	5		-	100 ± 8.9
Q	300.0	5	1	-	66.7 ± 11.3
	600.0	5		-	1.6 ± 1.5
	Ø	10		6.3	
ED ₅₀ (range) 330 (260 - 380)					
ED ₉₀ (range) 470 (360 - 530)					
Resistance factor I ₉₀ 15.2					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 30

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE... PARASITE (SUB)SPECIES *P. berghei*.....

FORMULATION ..Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC/PP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	60.0	5		-	64.0 ± 7.5
	100.0	5		-	27.8 ± 8.5
NH	300.0	5	1	-	0.01 ± 0.01
	600.0	5		-	0
	Ø	10		17.4	

ED₅₀(range) 72.0 (62.0 - 86.0)

ED₉₀(range) 117 (102 - 140)

Resistance factor I₉₀ 3.8

	30.0	5		-	86.3 ± 10.0
	100.0	5		-	88.9 ± 2.8
NAM	300.0	5	1	-	43.5 ± 11.7
	600.0	5		-	6.7 ± 5.2
	Ø	10		21.3	

ED₅₀(range) 240 (165 - 320)

ED₉₀(range) 550 (375 - 740)

Resistance factor I₉₀ 17.7

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 31

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC/HP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	60.0	5		-	56.9 ± 19.0
	100.0	5		-	3.1 ± 2.1
P	300.0	5	1	-	0
	∅	10		8.7	
ED ₅₀ (range) 62.0(54.0-73.0)					
ED ₉₀ (range) 85.0(74.0-100)					
Resistance factor I ₉₀ 2.7					
	30.0	5		-	15.6 ± 8.4
	100.0	5		-	2.4 ± 1.5
B	300.0	5	1	-	1.1 ± 0.4
	∅	10		20.4	
ED ₅₀ (range) 3.5(1.5-6.5)					
ED ₉₀ (range) 35.0(14.0-62.0)					
Resistance factor I ₉₀ 1.1					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 32

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC/IV/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	30.0	5		-	48.8 ± 13.5
	100.0	5		-	8.8 ± 5.2
PYR	300.0	5	1	-	0.6 ± 0.6
	Ø	10		23.1	

ED₅₀(range) 30.0(10.0-40.0)

ED₉₀(range) 93.0(33.0-125)

Resistance factor I₉₀ 3.0

	30.0	5		-	24.1 ± 7.7
	100.0	5		-	2.9 ± 1.3
ORA	300.0	5	1	-	0.1 ± 0.1
	Ø	10		13.7	

ED₅₀(range) 15.5(8.4 - 19.5)

ED₉₀(range) 54.0(28.5 - 67.0)

Resistance factor I₉₀ 1.7

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 33

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80 / H₂O... ROUTE OF ADMINISTRATION : SC/IV/PO/IV

MAXIMUM TOLERATED DOSE (MTO) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	60.0	5		-	89.4 ± 7.5
	100.0	5		-	76.5 ± 15.1
NPN	300.0	5	1	-	37.4 ± 8.1
	600.0	5		-	8.3 ± 5.1
	Ø	10		11.1	
ED ₅₀ (range) 200 (125 - 275)					
ED ₉₀ (range) 580 (370 - 810)					
Resistance factor I ₉₀ 18.7					
	60.0	5		-	55.7 ± 17.8
	100.0	5		-	3.9 ± 2.2
N 1708	300.0	5	1	-	0
	600.0	5		-	0
	Ø	10		10.7	
ED ₅₀ (range) 62.0 (54.0 - 72.0)					
ED ₉₀ (range) 88.0 (76.0 - 102)					
Resistance factor I ₉₀ 2.8					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 34

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE. PARASITE (SUB)SPECIES *P. berghei*.....

FORMULATION Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC/1P/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	30.0	5		-	100 ± 8.7
	100.0	5		-	20.0 ± 3.5
MFY	300.0	5	1	-	1.1 ± 0.8
	600.0	5		-	0
	Ø	10		7.1	
ED ₅₀ (range) 100(70.0-150)					
ED ₉₀ (range) 152(108-225)					
Resistance factor I ₉₀ 4.9					
	30.0	5		-	49.7 ± 9.9
	100.0	5		-	3.2 ± 0.9
KFY	300.0	5	1	-	0.2 ± 0.1
	600.0	5		-	0
	Ø	10		13.0	
ED ₅₀ (range) 27.0(20.0-36.0)					
ED ₉₀ (range) 71.0(55.0-95.0)					
Resistance factor I ₉₀ 2.3					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 35

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	30.0	5		-	72.9 ± 5.9
	100.0	5		-	27.5 ± 4.8
PFMA	300.0	5	1	-	0.3 ± 0.2
	600.0	5		-	0
	∅	10		21.4	

ED₅₀(range) 55.0(38.0 - 74.0)

ED₉₀(range) 127(86 - 170)

Resistance factor I₉₀ 4.1

	30.0	5		-	47.5 ± 2.2
	100.0	5		-	18.1 ± 7.0
N 1765	300.0	5	1	-	0.3 ± 0.2
	600.0	5		-	0
	∅	10		19.3	

ED₅₀(range) 35.0(22.5 - 58.0)

ED₉₀(range) 100(65.0 - 165)

Resistance factor I₉₀ 3.2

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 36

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80 / H₂O ROUTE OF ADMINISTRATION : SG/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	30.0	5		-	100 ± 5.0
	100.0	5		-	100 ± 10.1
QM	300.0	5	1	-	82.9 ± 7.8
	600.0	5		-	20.0 ± 7.8
	∅	10		4.2	

ED₅₀(range) 420 (380 - 480)

ED₉₀(range) 700 (620 - 800)

Resistance factor I₉₀

ED₅₀(range)

ED₉₀(range)

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 37

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE... PARASITE (SUB)SPECIES *P. berghei*.....

FORMULATION ... Tween 80/H₂O. ROUTE OF ADMINISTRATION : SC/++/PO/++

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x100
	60.0	5		-	79.2 ± 3.4
	100.0	5		-	58.4 ± 8.8
NS	300.0	5	1	-	0.3 ± 0.3
	600.0	5		-	0.2 ± 0.2
	∅	10		12.6	
ED ₅₀ (range) 100(43.0 - 145)					
EO ₉₀ (range) 195(83.0 - 280)					
Resistance factor I ₉₀ 6.5					
	60.0	5		-	58.1 ± 13.5
	100.0	5		-	23.7 ± 5.3
NS 1100	300.0	5	1	-	19.6 ± 5.7
	600.0	5		-	0.6 ± 0.4
	∅	10		5.4	
ED ₅₀ (range) 73.0(44.0 - 160)					
EO ₉₀ (range) 230(138 - 500)					
Resistance factor I ₉₀ 7.4					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 38

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE PARASITE (SUB)SPECIES P. yoelii.....

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/HP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	60.0	5		-	80.6 ± 6.1
	100.0	5		-	78.6 ± 12.3
SH	300.0	5	1	-	66.9 ± 6.1
	600.0	5		-	22.5 ± 13.6
	∅	10		7.2	
ED ₅₀ (range) 190(95.0 - 450)					
ED ₉₀ (range) 1050(540 - 2500)					
Resistance factor I ₉₀ 33.9					
	60.0	5		-	100 ± 3.5
	100.0	5		-	94.6 ± 7.5
SPN	300.0	5	1	-	89.5 ± 16.6
	600.0	5		-	14.1 ± 8.9
	∅	10		8.2	
ED ₅₀ (range) 430(200 - 1500)					
ED ₉₀ (range) 1000(470 - 3500)					
Resistance factor I ₉₀ 32.3					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 39

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE PARASITE (SUB)SPECIES P. yoelii

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x100
	30.0	5		-	60.4 ± 12.0
	100.0	5		-	30.9 ± 9.6
NS 1765	300.0	5	1	-	1.2 ± 0.6
	600.0	5		-	0
	∅	10		19.5	

ED₅₀(range) 50.0(28.5-85.0)

ED₉₀(range) 115(66.0-200)

Resistance factor I₉₀ 3.7

	30.0	5		-	84.7 ± 9.3
	100.0	5		-	1.3 ± 0.5
NS 1708	300.0	5	1	-	0.02 ± 0.02
	600.0	5		-	0
	∅	10		11.4	

ED₅₀(range) 37.5(28.0-51.0)

ED₉₀(range) 72.0(54.0-100)

Resistance factor I₉₀ 2.3

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 40

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE.. PARASITE (SUB)SPECIES P. yoelii.....

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION : SC/1P/PO/14

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	60.0	5		-	62.3 ± 5.4
	100.0	5		-	58.3 ± 10.9
QS	300.0	5	1	-	47.9 ± 4.7
	600.0	5		-	2.8 ± 2.2
	∅	10		20.2	
ED ₅₀ (range) 133 (67.0 - 315)					
ED ₉₀ (range) 385 (195 - 900)					
Resistance factor I ₉₀ 12.4					
	30.0	5		-	79.4 ± 9.4
	100.0	5		-	24.4 ± 6.1
NIG	300.0	5	1	-	0.1 ± 0.1
	600.0	5		-	0
	∅	10		21.3	
ED ₅₀ (range) 54.0 (35.0 - 74.0)					
ED ₉₀ (range) 115 (71.0 - 155)					
Resistance factor I ₉₀ 3.7					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLL 41

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE. PARASITE (SUB)SPECIES *P. yoelii*.....

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION : sc/tp/po/iv

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	60.0	5		-	94.5 ± 5.8
	100.0	5		-	61.7 ± 9.2
SAM	300.0	5	1	-	43.1 ± 12.5
	600.0	5		-	7.0 ± 3.5
	∅	10		21.4	
EO ₅₀ (range) 185(102 - 330)					
EO ₉₀ (range) 490(275 - 860)					
Resistance factor I ₉₀ 15.8					
	30.0	5		-	79.5 ± 12.2
	100.0	5		-	91.8 ± 3.9
MPS	300.0	5	1	-	60.9 ± 12.4
	600.0	5		-	7.3 ± 2.8
	∅	10		8.8	
EO ₅₀ (range) 270(200 - 440)					
EO ₉₀ (range) 620(445 - 1000)					
Resistance factor I ₉₀ 20.0					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 42

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	30.0	5		-	100 ± 1.8
	100.0	5		-	97.7 ± 6.5
QMS	300.0	5	1	-	93.7 ± 4.7
	600.0	5		-	64.8 ± 18.8
	∅	10		8.6	
ED ₅₀ (range) 1300(540 - 3500)		14,500)			
ED ₉₀ (range) 5400(2300 -					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 43

COMPOUND NAME

OR NUMBER

Mefloquine

PARASITE (SUB)SPECIES

P. berghei

FORMULATION

Tween 80/H₂O

ROUTE OF ADMINISTRATION :

SC/IV/PO/IV

MAXIMUM TOLERATED DOSE (MTD)

MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	3.0	5		-	86.0 ± 12.2
	10.0	5		-	63.3 ± 9.3
RC	30.0	5	1	-	57.9 ± 12.2
	100.0	5		-	21.7 ± 14.7
	∅	10		6.0	

ED₅₀(range) 25.5(12.0 - 80.0)

ED₉₀(range) 275(130 - 850)

Resistance factor I₉₀ 59.8

	3.0	5		-	13.8 ± 4.1
	10.0	5		-	3.8 ± 0.8
ORA	30.0	5	1	-	0.5 ± 0.3
	100.0	5		-	0.4 ± 0.3
	∅	10		14.1	

ED₅₀(range) 0.4(0.15 - 1.2)

ED₉₀(range) 4.2(1.5 - 12.0)

Resistance factor I₉₀ 0.9

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 44

COMPOUND NAME

OR NUMBER MEFLOQUINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	3.0	5		-	100 ± 4.4
	10.0	5		-	100
QM	30.0	5	1	-	87.1 ± 10.4
	100.0	5		-	62.1 ± 5.1
	Ø	10		8.7	
ED ₅₀ (range) <u>145(80.0 - 400)</u>					
ED ₉₀ (range) <u>850(480 - 2300)</u>					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

TABLE 45

OR NUMBER ..MEFLOQUINE..... PARASITE (SUB)SPECIES *P. yoelii* ssp.....

FORMULATION Tween 80/H₂O..... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLI 46

COMPOUND NAME

OR NUMBER

Mefloquine

PARASITE (SUB)SPECIES

P. yoelii

FORMULATION

Tween 80/H₂O

ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD)

MG/KG X ...

Strain	Daily dose . mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X 100
	3.0	5		-	11.4 ± 1.3
	10.0	5		-	7.0 ± 2.1
NIG	30.0	5	1	-	0.01 ± 0.01
	100.0	5		-	0
	∅	10		26.7	
ED ₅₀ (range) 1.6(0.9 - 2.9)					
ED ₉₀ (range) 5.2(2.8 - 9.3)					
Resistance factor I ₉₀ 1.1					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 4-7

COMPOUND NAME

OR NUMBER Halofantrine PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/1P/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	10.0	5		-	100 ± 7.1
	30.0	5		-	100 ± 12.8
RC	60.0	5	1	-	98.5 ± 7.8
	100.0	5		-	91.1 ± 9.2
	∅	10		5.4	
ED ₅₀ (range) > 100					
ED ₉₀ (range) > 100					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 48

COMPOUND NAME

OR NUMBER

Halofantrine

PARASITE (SUB)SPECIES *P. berghei*

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/TP/PQ/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	0.3	5		-	83.7 ± 11.8
	1.0	5		-	70.8 ± 12.5
RC	3.0	5	1	-	69.0 ± 16.0
	10.0	5		-	64.3 ± 11.5
	30.0	5		-	59.7 ± 5.4
	Ø	10		6.0	
ED ₅₀ (range)					
ED ₉₀ (range) > 30					
Resistance factor I ₉₀ > 27.3					
	0.3	5		-	94.1 ± 6.4
	1.0	5		-	39.7 ± 14.3
ORA	3.0	5	1	-	1.3 ± 0.9
	10.0	5		-	0.3 ± 0.3
	30.0	5		-	0
	Ø	10		14.1	
EO ₅₀ (range) 0.7 (0.3 - 1.3)					
EO ₉₀ (range) 1.9 (1.0 - 3.7)					
Resistance factor I ₉₀ 1.7					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 49

COMPOUND NAME

OR NUMBER

HALOFANTRINE

PARASITE (SUB)SPECIES *P. berghei*

FORMULATION *Twinn 80/H₂O* ROUTE OF ADMINISTRATION : SC ~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.3	5		-	63.8 ± 8.0
	1.0	5		-	37.7 ± 9.4
MFY	3.0	5	1	-	18.9 ± 9.4
	10.0	5		-	0.04 ± 0.04
	Ø	10		5.3	
ED ₅₀ (range) 0.8(0.3 - 1.9)					
ED ₉₀ (range) 2.0(0.9 - 5.0)					
Resistance factor I ₉₀					
	0.3	5		-	100 ± 3.8
	1.0	5		-	68.5 ± 16.7
KFY	3.0	5	1	-	2.8 ± 1.2
	10.0	5		-	0.3 ± 0.2
	30.0	5		-	0.03 ± 0.02
	Ø	10		7.8	
ED ₅₀ (range) 1.4(0.6 - 3.0)					
ED ₉₀ (range) 3.4(1.6 - 7.3)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 50

COMPOUND NAME

OR NUMBER

HALOFANTRINE

PARASITE (SUB)SPECIES *P. berghei*

FORMULATION *Twinn 80/H₂O* ROUTE OF ADMINISTRATION : SC/IV/PO/LV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.3	5		-	92.5 ± 3.7
	1.0	5		-	67.5 ± 16.7
NAM	3.0	5	1	-	48.9 ± 11.6
	10.0	5		-	41.4 ± 4.5
	30.0	5		-	26.9 ± 3.3
	∅	10		9.9	

ED₅₀(range) 4.6 (1.0 - 15.0)

ED₉₀(range) 30.0 (6.6 - 95.0)

Resistance factor I₉₀

	0.3	5		-	70.7 ± 10.6
	1.0	5		-	56.4 ± 3.7
MPS	3.0	5	1	-	79.4 ± 9.5
	10.0	5		-	100 ± 10.3
	30.0	5		-	64.8 ± 15.8
	∅	10		6.7	

ED₅₀(range) > 30

ED₉₀(range) » 30

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 51

COMPOUND NAME

DR NUMBER ...HALOFANTRINE..... PARASITE (SUB)SPECIES *P. berghei*.....

FORMULATION ...Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/1P/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	3.0	5		-	87.3 ± 5.6
	10.0	5		-	75.5 ± 4.2
QM	30.0	5	1	-	66.5 ± 6.0
	100.0	5		-	54.1 ± 11.4
	Ø	10		16.9	
ED ₅₀ (range) 105(30.0 - 315)					
ED ₉₀ (range) > 100					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

TABLE 52

OR NUMBER

HALOFANTRINE

PARASITE (SUB)SPECIES *P. berghei*....

FORMULATION : ~~Tween 80~~ / H₂O ROUTE OF ADMINISTRATION : SC / IP / PO / IV

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x100
	0.3	5		-	98.3 ± 13.9
	1.0	5		-	100 ± 9.9
QMS	3.0	5	1	-	100 ± 9.9
	10.0	5		-	100 ±
	30.0	5		-	88.6 ± 12.6
	∅	10		5.8	

ED₅₀(range) > 30ED₉₀(range) ➡ 30Resistance factor I_{90} ED₅₀(range)ED₉₀ (range)Resistance factor I_{90}

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 53

COMPOUND NAME

OR NUMBER

HALOFANTRINE.....

PARASITE (SUB)SPECIES **P. berghei**....

FORMULATION **Tween 80/H₂O** ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x100
	0.3	5		-	100 ± 3.2
	1.0	5		-	52.4 ± 10.7
PFMA	3.0	5	1	-	7.8 ± 2.2
	10.0	5		-	0
	Ø	10		9.5	
ED ₅₀ (range) 1.2(0.9 - 1.6)					
ED ₉₀ (range) 2.3(1.7 - 3.0)					
Resistance factor I ₉₀					
	0.3	5		-	82.7 ± 6.5
	1.0	5		-	66.1 ± 3.1
SAM	3.0	5	1	-	53.5 ± 5.0
	10.0	5		-	52.5 ± 5.1
	Ø	10		20.1	
ED ₅₀ (range) 3.8(1.4 - 13.8)					
ED ₉₀ (range) 60.0(22.0 - >100)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

TABLE 54

OR NUMBER HALOFANTRINE..... PARASITE (SUB)SPECIES P. yoelii ssp.

FORMULATION ..Tween 80../H₂O. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% $\times 100$				
	0.1	5		-	94.4 \pm 6.0				
	0.3	5		-	64.0 \pm 7.4				
QS	1.0	5	1	-	43.4 \pm 10.6				
	3.0	5		-	29.7 \pm 11.9				
	10.0	5		-	10.3 \pm 4.1				
	\emptyset	10		19.8					
EO ₅₀ (range) 0.9(0.4 - 1.9)									
EO ₉₀ (range) 6.5(2.9 - 14.5)									
Resistance factor I ₉₀ 5.9									
EO ₅₀ (range)									
EO ₉₀ (range)									
Resistance factor I ₉₀									

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TABLE 55

OR NUMBER Halofantrine PARASITE (SUB)SPECIES P. yoelii

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/~~IP~~/PO/IV

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3	5		-	87.3 ± 5.0
	1.0	5		-	67.2 ± 11.9
NIG	3.0	5	1	-	1.4 ± 0.4
	10.0	5		-	0.02 ± 0.01
	30.0	5		-	0
	∅	10			

$$ED_{50}(\text{range}) \ 0.8(0.5-1.8)$$
$$EO_{90}(\text{range}) 2.0(1.3 - 4.6)$$
Resistance factor I_{90} 1.8[illegible]ED₅₀(range)EO₉₀(range)Resistance factor I_{90}

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 56

COMPOUND NAME

OR NUMBER **MEPRACRINE** PARASITE (SUB)SPECIES **P. berghei**

FORMULATION **Tween 80/H₂O**.. ROUTE OF ADMINISTRATION : **SC/HP/PO/IV**

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.1	5		-	95.5 ± 4.9
	0.3	5		-	74.7 ± 12.3
N	1.0	5	1	-	21.7 ± 9.0
	3.0	5		-	6.3 ± 0.6
	10.0	5		-	0.4 ± 0.4
	30.0	5		-	0
	∅	10		9.4	
EO ₅₀ (range) 0.56(0.22 - 1.0)					
ED ₉₀ (range) 1.85(0.72 - 3.4)					
Resistance factor I ₉₀ 1.0					
	1.0	5		-	37.6 ± 9.9
	3.0	5		-	34.5 ± 7.0
RC	10.0	5	1	-	24.2 ± 9.9
	30.0	5		-	6.1 ± 2.3
	∅	10		3.3	
EO ₅₀ (range) 1.25(0.3 - 4.3)					
EO ₉₀ (range) 17.0(4.0 - 58.0)					
Resistance factor I ₉₀ 9.2					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 57

COMPOUND NAME

OR NUMBER MEPACRINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	1.0	5		-	100 ± 5.3
	3.0	5		-	87.6 ± 9.9
N 1100	10.0	5	1	-	69.0 ± 6.6
	30.0	5		-	39.3 ± 12.6
	Ø	10		2.9	
ED ₅₀ (range) 20.0 (9.7 - 33.0)					
ED ₉₀ (range) 195 (95.0 - 320)					
Resistance factor I ₉₀ 105					
	1.0	5		-	100 ±
	3.0	5		-	100 ±
Q	10.0	5	1	-	100 ± 11.9
	30.0	5		-	93.3 ± 5.8
	Ø	10		6.3	
ED ₅₀ (range)					
ED ₉₀ (range) > 30					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 58

COMPOUND NAME

OR NUMBER MEPACRINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/1P/PO/LV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	100
	3.0	5		-	70.1 ± 18.5
NH	10.0	5	1	-	0
	30.0	5		-	0
	∅	10		17.4	
ED ₅₀ (range) 3.4(2.9 - 5.1)					
ED ₉₀ (range) 4.7(4.1 - 7.2)					
Resistance factor I ₉₀ 2.5					
	0.3	5		-	100 ± 1.5
	1.0	5		-	96.9 ± 3.6
NAM	3.0	5	1	-	68.6 ± 16.1
	10.0	5		-	58.7 ± 6.4
	∅	10		21.3	
ED ₅₀ (range)					
ED ₉₀ (range) > 10					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 59

COMPOUND NAME

OR NUMBER .MEPACRINE..... PARASITE (SUB)SPECIES *P. berghei*....

FORMULATION .Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC, 4P/P0/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	63.9 ± 13.5
	3.0	5		-	34.5 ± 11.7
P	10.0	5	1	-	0
	30.0	5		-	0
	Ø	10		8.7	
ED ₅₀ (range) 1.53(0.97-2.8)					
ED ₉₀ (range) 2.9(1.8-5.2)					
Resistance factor I ₉₀ 1.6					
	0.3	5		-	100 ± 4.9
	1.0	5		-	80.7 ± 7.9
B	3.0	5	1	-	68.5 ± 18.3
	10.0	5		-	0.1 ± 0.1
	Ø	10		20.4	
ED ₅₀ (range) 2.2(1.15-5.4)					
ED ₉₀ (range) 4.6(2.4-11.5)					
Resistance factor I ₉₀ 2.5					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 60

COMPOUND NAME

OR NUMBER MEPACRINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION : SC/HP/PO/IV

MAXIMUM TOLERATED DOSE (MTO) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.3	5		-	36.4 ± 15.4
	1.0	5		-	17.2 ± 12.4
PYR	3.0	5	1	-	0.5 ± 0.4
	10.0	5		-	0
	Ø	10		23.1	

ED₅₀(range) 0.3(0.13 - 0.55)

ED₉₀(range) 1.05(0.47 - 2.0)

Resistance factor I₉₀ 0.6

	0.3	5		-	78.5 ± 6.9
	1.0	5		-	40.3 ± 12.9
ORA	3.0	5	1	-	26.3 ± 6.2
	10.0	5		-	0
	Ø	10		13.7	

ED₅₀(range) 0.95(0.42 - 2.3)

ED₉₀(range) 2.1(0.93 - 5.0)

Resistance factor I₉₀ 1.1

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 61

COMPOUND NAME

OR NUMBER MEPACRINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/TP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	88.6 ± 4.2
	3.0	5		-	83.4 ± 10.4
NPN	10.0	5	1	-	62.0 ± 10.0
	30.0	5		-	22.5 ± 15.3
	∅	10		11.1	

ED₅₀(range) 8.2(3.8 - 21.5)

ED₉₀(range) 45.0(21.0 - 118)

Resistance factor I₉₀ 24.3

	1.0	5		-	100 ± 2.1
	3.0	5		-	70.6 ± 16.7
N 1708	10.0	5	1	-	9.6 ± 3.7
	30.0	5		-	4.0 ± 2.0
	∅	10		20.6	

ED₅₀(range) 3.5(2.1 - 9.2)

ED₉₀(range) 12.3(7.3 - 32.5)

Resistance factor I₉₀ 6.6

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 62

COMPOUND NAME

OR NUMBER MEPACRINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/17/10/14

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	93.8 ± 8.4
	3.0	5		-	78.6 ± 12.7
MFY	10.0	5	1	-	0.03 ± 0.03
	30.0	5		-	0
	∅	10		7.1	

ED₅₀(range) 2.6(1.6 - 5.6)

EO₉₀(range) 4.8(3.0 - 10.4)

Resistance factor I₉₀ 2.6

	1.0	5		-	84.5 ± 7.4
	3.0	5		-	47.4 ± 17.7
KFY	10.0	5	1	-	0
	30.0	5		-	0
	∅	10		13.0	

ED₅₀(range) 2.0(1.3 - 3.5)

EO₉₀(range) 3.4(2.3 - 5.8)

Resistance factor I₉₀ 1.8

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 63

COMPOUND NAME

OR NUMBER MEPACRINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	1.0	5		-	99.7 ± 4.0
	3.0	5		-	86.0 ± 1.7
PFMA	10.0	5	1	-	15.1 ± 6.1
	30.0	5		-	4.3 ± 1.3
	∅	10		21.4	
EO ₅₀ (range) 6.6 (3.9 - 10.0)					
EO ₉₀ (range) 16.0 (9.2 - 24.4)					
Resistance factor I ₉₀ 8.6					
	1.0	5		-	94.0 ± 7.8
	3.0	5		-	97.8 ± 2.5
N 1765	10.0	5	1	-	79.0 ± 3.1
	30.0	5		-	13.4 ± 7.7
	∅	10		19.3	
EO ₅₀ (range) 15.0 (6.0 - 20.0)					
EO ₉₀ (range) 38.0 (15.5 - 51.0)					
Resistance factor I ₉₀ 20.5					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 64

COMPOUND NAME

OR NUMBER ...MEPACRINE..... PARASITE (SUB)SPECIES *P. berghei*.....

FORMULATION *Tween 80/H₂O*... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	100 ± 0.5
	3.0	5		-	98.6 ± 5.5
QM	10.0	5	1	-	82.4 ± 8.7
	30.0	5		-	71.0 ± 9.6
	∅	10		4.2	
ED ₅₀ (range) > 30					
ED ₉₀ (range) >> 30					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDALS)

TABLE 65

COMPOUND NAME

OR NUMBER

MEPACRINE

PARASITE (SUB)SPECIES *P. yoelii*

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/1P/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg DD-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	78.1 ± 5.9
	3.0	5		-	55.9 ± 13.4
NS	10.0	5	1	-	16.4 ± 8.2
	30.0	5		-	11.4 ± 5.5
	Ø	10		23.3	

ED₅₀(range) 3.6(1.7 - 5.5)

ED₉₀(range) 18.3(8.5 - 28.0)

Resistance factor I₉₀ 9.9

	1.0	5		-	73.7 ± 11.0
	3.0	5		-	73.0 ± 1.4
NS 1100	10.0	5	1	-	53.3 ± 8.9
	30.0	5		-	30.4 ± 7.8
	Ø	10		5.4	

ED₅₀(range) 10.0(7.0 - 16.5)

ED₉₀(range) 120(82.0 - 190)

Resistance factor I₉₀ 64.9

Principal Investigator: Professor W. Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 66

COMPOUND NAME

OR NUMBER

MEPACRINE

PARASITE (SUB)SPECIES

P. yoelii

FORMULATION

Tween 80/H₂O

ROUTE OF ADMINISTRATION : SC/IV/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	96.5 ± 8.4
	3.0	5		-	100 ± 5.7
SH	10.0	5	1	-	81.1 ± 9.1
	30.0	5		-	38.9 ± 9.4
	Ø	10		5.7	

ED₅₀(range) 22.5(17.5-29.0)

ED₉₀(range) 78.0(59.0-100)

Resistance factor I₉₀ 42.2

	1.0	5		-	100 ± 6.6
	3.0	5		-	86.9 ± 7.8
SPN	10.0	5	1	-	80.6 ± 16.8
	30.0	5		-	80.9 ± 11.7
	Ø	10		6.4	

ED₅₀(range)

ED₉₀(range) > 30

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 67

COMPOUND NAME

OR NUMBER

MEPACRINE

PARASITE (SUB)SPECIES *P. yoelii*

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION: SC/~~IP~~/~~PO~~/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	99.1 ± 1.6
	3.0	5		-	88.0 ± 9.6
NS 1765	10.0	5	1	-	19.1 ± 4.5
	30.0	5		-	9.5 ± 5.6
	∅	10		19.5	
ED ₅₀ (range) 7.0(3.6 - 19.5)					
ED ₉₀ (range) 23.5(12.0 - 65.0)					
Resistance factor I ₉₀ 12.7					
	0.3	5		-	88.6 ± 7.2
	1.0	5		-	73.5 ± 10.8
NS 1708	3.0	5	1	-	63.0 ± 9.3
	10.0	5		-	13.5 ± 7.2
	∅	10		11.4	
ED ₅₀ (range) 2.1(0.9 - 6.4)					
ED ₉₀ (range) 11.8(5.2 - 36.0)					
Resistance factor I ₉₀ 6.4					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 68

COMPOUND NAME

OR NUMBER ... MEPA CRINE ... PARASITE (SUB) SPECIES *P. yoelii* ...

FORMULATION ... Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/~~IP~~/~~PO~~/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	98.0 ± 2.1
	3.0	5		-	73.1 ± 8.1
QS	10.0	5	1	-	60.4 ± 8.7
	30.0	5		-	47.3 ± 8.7
	∅	10		20.2	
ED ₅₀ (range)					
ED ₉₀ (range) > 30					
Resistance factor I ₉₀					
	0.3	5		-	95.2 ± 2.0
	1.0	5		-	59.7 ± 7.0
NIG	3.0	5	1	-	48.7 ± 5.2
	10.0	5		-	24.9 ± 7.2
	∅	10		21.3	
ED ₅₀ (range) 2.2 (0.9 - 5.0)					
ED ₉₀ (range) 13.0 (5.1 - 29.0)					
Resistance factor I ₉₀ 7.0					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 69

COMPOUND NAME

OR NUMBER

Mepacrine

PARASITE (SUB)SPECIES *P. yoelii*

FORMULATION *Tween 80/H₂O* ROUTE OF ADMINISTRATION : SC ~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	10.0	5		-	86.2 ± 6.4
	30.0	5		-	59.3 ± 5.0
QS	60.0	5	1	-	52.0 ± 4.9
	100.0	5		-	23.7 ± 6.5
	∅	10		18.0	
ED ₅₀ (range) 47.0(28.0 - 77.0)					
ED ₉₀ (range) 250(145 - 410)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 70

COMPOUND NAME

OR NUMBER MEPACRINE PARASITE (SUB)SPECIES P. yoelii

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/1P/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	100 ± 0.4
	3.0	5		-	99.5 ± 2.2
SAM	10.0	5	1	-	48.0 ± 7.2
	30.0	5		-	43.1 ± 7.2
	Ø	10		21.4	
ED ₅₀ (range)					
ED ₉₀ (range) > 30					
Resistance factor I ₉₀					
	0.3	5		-	88.9 ± 6.3
	1.0	5		-	98.4 ± 3.7
MPS	3.0	5	1	-	81.4 ± 5.9
	10.0	5		-	59.3 ± 9.6
	Ø	10		8.8	
ED ₅₀ (range)					
ED ₉₀ (range) > 10					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 71

COMPOUND NAME

OR NUMBER

MEPACRINE

PARASITE (SUB)SPECIES

P. berghei

FORMULATION

Tween 80/H₂O

ROUTE OF ADMINISTRATION :

SC/1P/10/14

MAXIMUM TOLERATED DOSE (MTD)

MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	0.3	5		-	95.1 ± 8.9
	1.0	5		-	85.6 ± 6.9
QMS	3.0	5	1	-	91.9 ± 3.3
	10.0	5		-	93.3 ± 3.3
	Ø	10		8.6	
ED ₅₀ (range) > 10					
ED ₉₀ (range) » 10					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 72

COMPOUND NAME

OR NUMBER Artemisinin PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H₂O ... ROUTE OF ADMINISTRATION : SC/IP/PQ/IV

MAXIMUM TOLERATED DOSE (MTO) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	3.0	5		-	100 ± 4.8
	10.0	5		-	61.7 ± 11.5
RC	30.0	5	1	-	49.3 ± 15.7
	100.0	5		-	24.7 ± 9.9
	∅	10		6.0	
ED ₅₀ (range) 26.0 (8.5 - 70.0)					
ED ₉₀ (range) 430 (165 - >1000)					
Resistance factor I ₉₀ 102					
	3.0	5		-	86.4 ± 4.4
	10.0	5		-	0.7 ± 0.4
ORA	30.0	5	1	-	0.01 ± 0.01
	100.0	5		-	0
	∅	10			
ED ₅₀ (range) 4.6 (3.4 - 6.5)					
ED ₉₀ (range) 7.5 (5.4 - 10.6)					
Resistance factor I ₉₀ 1.8					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 73

COMPOUND NAME

OR NUMBER

...ARTEMISININ.....

PARASITE (SUB)SPECIES

...P. berghei.....

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/~~IP~~/~~PO~~/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	10.0	5		-	51.1 ± 9.2
	30.0	5		-	47.3 ± 10.9
QM	100.0	5	1	-	5.3 ± 3.0
	300.0	5		-	0.02 ± 0.01
	∅	10		16.9	
ED ₅₀ (range) <u>18.5 (8.5 - 34.0)</u>					
ED ₉₀ (range) <u>52.0 (23.5 - 95.0)</u>					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 74

COMPOUND NAME

DR NUMBER **ARTEMISININ**..... PARASITE (SUB)SPECIES **P. berghei**....

FORMULATION **Tween 80 / H₂O** ROUTE OF ADMINISTRATION : SC/~~IP~~/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg DO-3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ¹⁰⁰
	3.0	5		-	79.3 ± 5.1
	10.0	5		-	20.0 ± 6.9
NS 1100	30.0	5	1	-	1.1 ± 0.3
	100.0	5		-	0.04 ± 0.03
	Ø	10		5.6	
ED ₅₀ (range) 5.3(4.1 - 6.3)					
ED ₉₀ (range) 13.8(10.8 - 17.0)					
Resistance factor I ₉₀					
	3.0	5		-	81.1 ± 2.0
	10.0	5		-	54.4 ± 7.1
SAM	30.0	5	1	-	22.8 ± 4.2
	100.0	5		-	0
	Ø	10		22.2	
ED ₅₀ (range) 10.2(4.7 - 20.0)					
ED ₉₀ (range) 22.5(10.2 - 44.0)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 75

COMPOUND NAME

OR NUMBER ..ARTEMISININ..... PARASITE (SUB)SPECIES *P. yoelii* ssp..

FORMULATION *Tween 80/H₂O*.. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	3.0	5		-	75.8 ± 11.0
	10.0	5		-	52.3 ± 8.5
QS	30.0	5	1	-	29.9 ± 11.3
	100.0	5		-	17.4 ± 6.8
	∅	10		19.8	
ED ₅₀ (range) 11.8(6.5 - 24.0)					
ED ₉₀ (range) 165(90.0 - 330)					
Resistance factor I ₉₀ 33.3					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 76

COMPOUND NAME

OR NUMBER Artemisinin PARASITE (SUB)SPECIES P. yoelii

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/ID/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	3.0	5		-	96.8 ± 2.1
	10.0	5		-	48.6 ± 8.8
NIG	30.0	5	1	-	0
	100.0	5		-	0
	∅	10			
ED ₅₀ (range) 7.2 (5.1 - 10.6)					
ED ₉₀ (range) 11.5 (8.1 - 17.0)					
Resistance factor I ₉₀ 2.7					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 77

COMPOUND NAME

OR NUMBER **ARTEMISININ**..... PARASITE (SUB)SPECIES **P. berghei**....

FORMULATION **Tween 80 / H₂O**. ROUTE OF ADMINISTRATION : **SC / IP / PO / IV**

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	3.0	5		-	100 ± 6.0
	10.0	5		-	82.1 ± 11.6
QMS	30.0	5	1	-	70.7 ± 10.3
	100.0	5		-	6.9 ± 3.0
	∅	10		5.8	
ED ₅₀ (range) 35.0 (17.0 - 68.0)					
ED ₉₀ (range) 120 (57.0 - 245)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 78

COMPOUND NAME

OR NUMBER ... **PYRONARIDINE** ... PARASITE (SUB)SPECIES ... **P. berghei** ...

FORMULATION **Tween 80/H₂O**. ROUTE OF ADMINISTRATION : SC/~~IP~~/~~PO~~/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.3	5		-	96.4 ± 3.2
	1.0	5		-	6.2 ± 3.4
MFY	3.0	5	1	-	0.01 ± 0.01
	10.0	5		-	0
	Ø	10		8.4	
ED ₅₀ (range) 0.6(0.5 - 0.8)					
ED ₉₀ (range) 0.9(0.7 - 1.3)					
Resistance factor I ₉₀					
	0.3	5		-	84.9 ± 5.0
	1.0	5		-	1.3 ± 1.2
KFY	3.0	5	1	-	0.01 ± 0.01
	10.0	5		-	0
	Ø	10		9.3	
ED ₅₀ (range) 0.4(0.3 - 0.5)					
ED ₉₀ (range) 0.7(0.5 - 0.8)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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TABLE 79

OR NUMBER ...PYRONARIDINE..... PARASITE (SUB)SPECIES *P. yacuii* spp...

FORMULATION ...Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ¹⁰⁰				
	0.1	5		-	100 ± 3.4				
	0.3	5		-	92.8 ± 7.4				
QS	1.0	5	1	-	58.1 ± 12.4				
	3.0	5		-	35.5 ± 3.7				
	10.0	5		-	26.5 ± 7.5				
	Ø	10		19.8					
ED ₅₀ (range) 2.4(0.8 - 5.2)									
ED ₉₀ (range) 19.5(6.8 - 42.0)									
Resistance factor I ₉₀ 27.5									
ED ₅₀ (range)									
ED ₉₀ (range)									
Resistance factor I ₉₀									

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 80

COMPOUND NAME

OR NUMBER ..PYRONARIDINE..... PARASITE (SUB)SPECIES *P. berghei*.....

FORMULATION *Tween 80/H₂O*. ROUTE OF ADMINISTRATION : SC/ID/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3	5		-	100 ± 2.6
	1.0	5		-	63.5 ± 9.2
SAM	3.0	5	1	-	33.1 ± 16.5
	10.0	5		-	0.3 ± 0.3
	Ø	10		12.7	
ED ₅₀ (range) 1.6(1.0 - 3.0)					
ED ₉₀ (range) 3.2(2.0 - 6.0)					
Resistance factor I ₉₀					
	0.3	5		-	66.3 ± 11.3
	1.0	5		-	74.2 ± 5.2
MPS	3.0	5	1	-	80.4 ± 5.7
	10.0	5		-	22.5 ± 5.4
	Ø	10		10.4	
ED ₅₀ (range) 5.6(4.7 - 6.7)					
ED ₉₀ (range) 14.3(12.0 - 17.5)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 81

COMPOUND NAME

OR NUMBER ... PYRPHORIDINE ... PARASITE (SUB)SPECIES P. berghei ...

FORMULATION Tween 80/H₂O ... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3	5		-	81.9 ± 5.4
	1.0	5		-	73.3 ± 14.5
QMS	3.0	5	1	-	53.5 ± 11.6
	10.0	5		-	46.5 ± 10.7
	Ø	10		8.6	
ED ₅₀ (range) <u>3.5(1.3 - 12.0)</u>					
ED ₉₀ (range) <u>46.0(17.5 - >100)</u>					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 82

COMPOUND NAME

OR NUMBER PYRIMETHAMINE PARASITE (SUB)SPECIES *P. berghei*

FORMULATION *Tween 80 / H₂O* ... ROUTE OF ADMINISTRATION : *SC/IP/PO/IV*

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	0.3	5		-	80.2 ± 4.1
	1.0	5		-	65.9 ± 14.8
B	3.0	5	1	-	25.0 ± 9.9
	10.0	5		-	0.01 ± 0.01
	30.0	5		-	0
	∅	10		24.6	
ED ₅₀ (range) 1.2(0.4 - 2.4)					
ED ₉₀ (range) 2.4(0.9 - 5.0)					
Resistance factor I ₉₀					
	1.0	5		-	72.5 ± 11.1
	3.0	5		-	20.2 ± 9.5
PYR	10.0	5	1	-	0.1 ± 0.1
	30.0	5		-	0
	∅	10		19.9	
ED ₅₀ (range) 1.5(1.0 - 2.1)					
ED ₉₀ (range) 3.4(2.2 - 4.7)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 83

COMPOUND NAME

OR NUMBER Pyrimethamine..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O.... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.03	5		-	44.5 ± 13.1
	0.1	5		-	0.7 ± 0.3
QM	0.3	5	1	-	0
	1.0	5		-	0
	Ø	10		16.9	
EO ₅₀ (range) <u>0.028(0.022 - 0.032)</u>					
EO ₉₀ (range) <u>0.054(0.043 - 0.062)</u>					
Resistance factor I ₉₀					
EO ₅₀ (range)					
EO ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 84

COMPOUND NAME

OR NUMBER PYRIMETHAMINE PARASITE (SUB)SPECIES *P. yoelii* ssp..

FORMULATION ... Tween 80 / H₂O ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	0.03	5		-	15.2 ± 12.9
	0.1	5		-	3.3 ± 2.6
QS	0.3	5	1	-	0.7 ± 0.3
	1.0	5		-	0
	∅	10		19.8	

ED₅₀(range) 0.007(0.002 - 0.01)

ED₉₀(range) 0.045(0.016 - 0.085)

Resistance factor I₉₀ 0.38

	0.03	5		-	70.0 ± 16.0
	0.1	5		-	9.6 ± 8.0
NS 1100	0.3	5	1	-	0
	1.0	5		-	0
	∅	10		4.8	

ED₅₀(range) 0.043(0.031 - 0.06)

ED₉₀(range) 0.083(0.06 - 0.12)

Resistance factor I₉₀ 0.09

Principal Investigator: Professor W. Peters
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TABLE 85

OR NUMBER ..SULFADOXINE..... PARASITE (SUB)SPECIES *P. berghei*.....

FORMULATION Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% $\times 100$				
	0.1	5		-	92.7 \pm 3.2				
	0.3	5		-	55.0 \pm 19.0				
PYR	1.0	10	2	-	15.8 \pm 8.2				
	3.0	10		-	1.4 \pm 0.9				
	10.0	5		-	0.02 \pm 0.01				
	30.0	5		-	0				
	ϕ	20		21.8					
ED ₅₀ (range) 0.36 (0.21 - 0.55)									
ED ₉₀ (range) 1.15 (0.67 - 1.8)									
Resistance factor I ₉₀									
ED ₅₀ (range)									
ED ₉₀ (range)									
Resistance factor I ₉₀									

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 86

COMPOUND NAME

OR NUMBER SULFADOXINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	0.03	5		-	76.6 ± 12.5
	0.1	5		-	21.0 ± 19.0
QM	0.3	5	1	-	0.5 ± 0.5
	1.0	5		-	0
	Ø	10		16.9	
ED ₅₀ (range) 0.05(0.02 - 0.08)					
ED ₉₀ (range) 0.12(0.05 - 0.2)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 87

COMPOUND NAME

OR NUMBER ... SULFADOXINE ... PARASITE (SUB)SPECIES P. yoelii ssp.

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/IV/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.03	5		-	43.2 ± 8.6
	0.1	5		-	0.6 ± 0.3
QS	0.3	5	1	-	0
	1.0	5		-	0
	Ø	10		19.8	
ED ₅₀ (range) 0.028 (0.024 - 0.032)					
ED ₉₀ (range) 0.052 (0.045 - 0.06)					
Resistance factor I ₉₀ 0.01					
	0.03	5		-	72.9 ± 15.2
	0.1	5		-	3.8 ± 3.6
NS 1100	0.3	5	1	-	0
	1.0	5		-	0
	Ø	10		4.8	
ED ₅₀ (range) 0.041 (0.029 - 0.053)					
ED ₉₀ (range) 0.076 (0.044 - 0.1)					
Resistance factor I ₉₀ 0.02					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 88

COMPOUND NAME

OR NUMBER PYRIMETHAMINE: SULFADOXINE (1:3) PARASITE (SUB)SPECIES *P. berghei*

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION: SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.01	5		-	96.7 ± 5.6
	0.03	5		-	83.5 ± 5.2
P	0.1	5	2	-	82.2 ± 8.1
	0.3	10		-	37.5 ± 6.5
	1.0	5		-	0
	∅	20		9.0	
ED ₅₀ (range) 0.07 (0.03 - 0.25)					
ED ₉₀ (range) 0.2 (0.07 - 0.6)					
Resistance factor I ₉₀					
	0.3	5		-	68.0 ± 12.0
	1.0	5		-	0.08 ± 0.08
B	3.0	5	1	-	0
	10.0	5		-	0
	∅	10		24.5	
ED ₅₀ (range) 0.34 (0.28 - 0.4)					
ED ₉₀ (range) 0.52 (0.42 - 0.6)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

TABLE 89

OR NUMBER PYRIMETHAMINS: SULFADIXINE (1:3) PARASITE (SUB) SPECIES *P. berghei*.....

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% $\times 100$
	0.1	5		-	92.3 \pm 3.6
	0.3	10		-	54.4 \pm 9.9
PYR	1.0	5	2	-	2.1 \pm 0.7
	3.0	5		-	0
	ϕ	20		21.8	

ED₅₀(range) 0.26(0.21-0.38)

ED₉₀(range) 0.6 (0.49 - 0.86)

Resistance factor I_{90} ED₅₀(range)ED₉₀ (range)Resistance factor I_{90}

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 90

COMPOUND NAME 1:3

OR NUMBER PYRIMETHAMINE: SULFADOXINE PARASITE (SUB)SPECIES *P. berghei*.....

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/IP/P0/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X 100
	0.03	5		-	62.1 ± 3.2
	0.1	5		-	0.2 ± 0.1
QM	0.3	5	1	-	0
	1.0	5		-	0
	Ø	10		16.9	
ED ₅₀ (range) 0.033(0.029 - 0.037)					
ED ₉₀ (range) 0.052(0.046 - 0.06)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 91

COMPOUND NAME

OR NUMBER PYRIMETHAMINE : SULFADOXINE (1:3) PARASITE (SUB)SPECIES *P. yoelii* ssp..

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION : ~~SC~~ IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x100
	0.01	5		-	50.1 ± 18.9
	0.03	5		-	37.0 ± 8.9
QS	0.1	5	1	-	0.9 ± 0.9
	0.3	5		-	0
	Ø	10		19.8	
EO ₅₀ (range) 0.015(0.006 - 0.027)					
EO ₉₀ (range) 0.052(0.02 - 0.094)					
Resistance factor I ₉₀ 0.16					
	0.01	5		-	100 ± 4.0
	0.03	5		-	86.3 ± 18.8
NS 1100	0.1	5	1	-	22.5 ± 19.6
	0.3	5		-	0
	Ø	10		4.8	
EO ₅₀ (range) 0.06(0.04 - 0.085)					
EO ₉₀ (range) 0.14(0.09 - 0.2)					
Resistance factor I ₉₀ 0.44					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 92

COMPOUND NAME

OR NUMBER

..CYCLOSPONIL.....

PARASITE (SUB)SPECIES *P. berghei*....

FORMULATION *Tween 80 / H₂O* ROUTE OF ADMINISTRATION : SC/~~IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	10.0	5		-	97.3 ± 4.4
	30.0	5		-	78.3 ± 8.4
P	60.0	5	1	-	61.7 ± 8.4
	100.0	5		-	41.1 ± 8.4
	Ø	10		14.1	

ED₅₀(range) 75.0(50.0 - 110)

ED₉₀(range) 320(220 - 460)

Resistance factor I₉₀

	10.0	5		-	88.9 ± 4.3
	30.0	5		-	85.4 ± 2.6
B	60.0	5	1	-	77.3 ± 3.5
	100.0	5		-	77.3 ± 4.6
	Ø	10		28.4	

ED₅₀(range) >100

ED₉₀(range) >100

Resistance factor I₉₀

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 93

COMPOUND NAME

OR NUMBER **CYCLOQUANIL**..... PARASITE (SUB)SPECIES **P. berghei**....

FORMULATION **Tween 80/H₂O** ROUTE OF ADMINISTRATION : **SC/IV/PO/IV**

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	10.0	5		-	91.8 ± 2.6
	30.0	5		-	90.9 ± 1.0
PYR	60.0	5	1	-	90.9 ± 2.4
	100.0	5		-	74.6 ± 5.5
	Ø	10		27.6	
ED ₅₀ (range) > 100					
ED ₉₀ (range) » 100					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 94

COMPOUND NAME

OR NUMBER ...CYCLOGUANIL..... PARASITE (SUB)SPECIES ...*P. berghei*....

FORMULATION ...Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/~~IP~~/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3	5		-	81.4 ± 9.0
	1.0	5		-	56.3 ± 8.6
QM	3.0	5	1	-	9.6 ± 3.4
	10.0	5		-	3.3 ± 1.6
	∅	10		16.9	
ED ₅₀ (range) 1.0(0.5 - 1.7)					
ED ₉₀ (range) 4.0(2.1 - 6.6)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 95

COMPOUND NAME

OR NUMBER CYCLOQUANIL PARASITE (SUB)SPECIES P. yoelii sp...

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/IP/PQ/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3	5		-	69.4 ± 8.4
	1.0	5		-	41.3 ± 7.2
QS	3.0	5	1	-	32.3 ± 4.5
	10.0	5		-	3.5 ± 2.8
	∅	10		19.8	
ED ₅₀ (range) 0.9(0.2 - 1.9)					
ED ₉₀ (range) 6.3(1.6 - 12.8)					
Resistance factor I ₉₀ 1.9					
	0.3	5		-	83.3 ± 8.4
	1.0	5		-	47.9 ± 11.2
NS 1100	3.0	5	1	-	14.6 ± 6.4
	10.0	5		-	4.6 ± 2.4
	∅	10		4.8	
ED ₅₀ (range) 0.9(0.7 - 1.4)					
ED ₉₀ (range) 4.8(3.6 - 8.0)					
Resistance factor I ₉₀ 1.5					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 96

COMPOUND NAME

OR NUMBER

...MENOCTONE.....

PARASITE (SUB)SPECIES *P. yoelii* ssp

FORMULATION *Tween 80/H₂O*. ROUTE OF ADMINISTRATION : SC/HP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x100
	0.3	5		-	69.9 ± 9.0
	1.0	5		-	49.5 ± 3.3
QS	3.0	5	1	-	0.01 ± 0.01
	10.0	5		-	0
	∅	10		19.8	
ED ₅₀ (range) 0.6 (0.35 - 1.0)					
ED ₉₀ (range) 1.2 (0.7 - 2.1)					
Resistance factor I ₉₀ 0.86					
	0.3	5		-	89.2 ± 17.2
	1.0	5		-	72.9 ± 17.6
NS 1100	3.0	5	1	-	2.9 ± 1.6
	10.0	5		-	0
	∅	10		4.8	
ED ₅₀ (range) 1.1 (0.5 - 2.6)					
ED ₉₀ (range) 3.1 (1.4 - 6.6)					
Resistance factor I ₉₀ 2.2					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIOES)

TABLE 97

COMPOUND NAME

OR NUMBER .. **FLOXACINE**..... PARASITE (SUB)SPECIES **P. berghei**....

FORMULATION **Tween 80 / H₂O** ROUTE OF ADMINISTRATION : SC/~~IP~~/~~PO~~/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.1	5		-	82.3 ± 9.5
	0.3	5		-	59.6 ± 9.1
PFMA	1.0	5	1	-	0.01 ± 0.01
	3.0	5		-	0
	Ø	10		14.6	

EO₅₀(range) **0.2(0.1 - 0.4)**

EO₉₀(range) **0.4(0.2 - 0.6)**

Resistance factor I₉₀

	0.1	5		-	92.8 ± 7.8
	0.3	5		-	78.8 ± 7.3
NAM	1.0	5	1	-	0.9 ± 0.7
	3.0	5		-	0.01 ± 0.01
	Ø	10		11.6	

EO₅₀(range) **0.3(0.2 - 0.6)**

EO₉₀(range) **0.7(0.4 - 1.2)**

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIOES)

TABLE 98

COMPOUND NAME

OR NUMBER ... **FLOXASINE** ... PARASITE (SUB)SPECIES **P. berghei** ...

FORMULATION **Tween 80/H₂O** ROUTE OF ADMINISTRATION : **SC/IP/PO/IV**

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.1	5		-	100 ± 4.1
	0.3	5		-	100 ± 0.4
QM	1.0	5	-	-	0.5 ± 0.4
	3.0	5		-	0
	∅	10		8.8	
EO ₅₀ (range) 0.6(0.5 - 0.7)					
EO ₉₀ (range) 0.7(0.6 - 0.8)					
Resistance factor I ₉₀					
EO ₅₀ (range)					
EO ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 99

COMPOUND NAME

OR NUMBER ... FLOXACRINE ... PARASITE (SUB)SPECIES ... P. yoelii ssp.

FORMULATION ... Tween 80/H₂O ... ROUTE OF ADMINISTRATION : SC/1P/10/11

MAXIMUM TOLERATED DOSE (MTD) ... MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.03	5		-	67.8 ± 8.6
	0.1	5		-	52.1 ± 3.8
QS	0.3	5	1	-	40.7 ± 3.9
	1.0	5		-	0.4 ± 0.3
	Ø	10		19.8	
EO ₅₀ (range) 0.1 (0.037 - 0.28)					
EO ₉₀ (range) 0.31 (0.11 - 0.82)					
Resistance factor I ₉₀ 0.31					
	0.03	5		-	95.0 ± 6.4
	0.1	5		-	100 ± 3.6
NS 1100	0.3	5	1	-	60.8 ± 13.6
	1.0	5		-	0
	Ø	10		4.8	
EO ₅₀ (range) 0.32 (0.28 - 0.36)					
EO ₉₀ (range) 0.47 (0.42 - 0.53)					
Resistance factor I ₉₀ 0.47					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 100

COMPOUND NAME

OR NUMBER ...CLINDAMYCIN..... PARASITE (SUB)SPECIES *P. yoelii* ssp....

FORMULATION ..Tween 80./H₂O.. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	3.0	5		-	33.4 ± 8.9
	10.0	5		-	20.4 ± 8.1
QS	30.0	5	1	-	0.3 ± 0.3
	100.0	5		-	0
	∅	10		19.8	
ED ₅₀ (range) 2.9 (0.7 - 5.6)					
ED ₉₀ (range) 10.0 (2.6 - 20.0)					
Resistance factor I ₉₀ 0.3					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 104

COMPOUND NAME

OR NUMBER DOXYCYCLINE PARASITE (SUB)SPECIES *P. berghei*

FORMULATION *Tween 80/H₂O* ... ROUTE OF ADMINISTRATION : SC/~~IP/PO~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PMS Control PMS
	0.1	5		-	58.9 ± 6.9
	0.3	5		-	57.4 ± 19.2
N	1.0	5	1	-	36.6 ± 13.7
	3.0	5		-	27.7 ± 13.5
	10.0	5		-	0.9 ± 0.4
	30.0	5		-	0
	∅	10		9.4	
EO ₅₀ (range) 0.5(0.2 - 2.2)					
EO ₉₀ (range) 2.7(1.0 - 12.0)					
Resistance factor I ₉₀ 1.0					
	0.1	5		-	81.8 ± 15.1
	0.3	5		-	69.7 ± 14.0
RC	1.0	5	1	-	38.8 ± 11.6
	3.0	5		-	11.6 ± 9.9
	∅	10		3.3	
EO ₅₀ (range) 0.5(0.2 - 1.3)					
EO ₉₀ (range) 3.8(1.4 - 10.0)					
Resistance factor I ₉₀ 1.4					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 102

COMPOUND NAME

OR NUMBER DOXYCYCLINE PARASITE (SUB)SPECIES *P. berghei*

FORMULATION *Tween 80/H₂O* .. ROUTE OF ADMINISTRATION : SC/10/10/11

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3	5		-	100 ± 5.3
	1.0	5		-	84.4 ± 4.6
N 1100	3.0	5	1	-	79.3 ± 18.5
	10.0	5		-	40.0 ± 17.9
	∅	10		2.9	
ED ₅₀ (range) 7.4 (3.8 - 12.5)					
ED ₉₀ (range) 33.0 (16.0 - 53.0)					
Resistance factor I ₉₀ 12.2					
	0.1	5		-	100 ± 1.8
	0.3	5		-	95.6 ± 9.8
Q	1.0	5	1	-	89.2 ± 6.4
	3.0	5		-	55.2 ± 14.0
	10.0	5		-	8.8 ± 5.2
	∅	10		6.3	
ED ₅₀ (range) 3.0 (2.3 - 4.6)					
ED ₉₀ (range) 9.3 (7.1 - 14.5)					
Resistance factor I ₉₀ 3.4					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 103

COMPOUND NAME

OR NUMBER DOXYCYCLINE PARASITE (SUB)SPECIES *P. berghei*

FORMULATION *Tween 80/H₂O*... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3	5		-	100
	1.0	5		-	100 ± 1.7
NH	3.0	5	1	-	84.9 ± 9.4
	10.0	5		-	38.3 ± 7.2
	30.0	5		-	3.3 ± 0.8
	∅	10		17.4	
EO ₅₀ (range) 6.1 (4.9 - 9.0)					
EO ₉₀ (range) 20.0 (13.5 - 25.0)					
Resistance factor I ₉₀ 7.4					
	0.1	5		-	85.4 ± 5.0
	0.3	5		-	90.5 ± 5.8
NAM	1.0	5	1	-	86.8 ± 2.9
	3.0	5		-	76.5 ± 8.6
	10.0	5		-	46.9 ± 12.2
	∅	10		21.3	
EO ₅₀ (range) 9.5 (7.0 - 19.5)					
EO ₉₀ (range) 115 (85.0 - 235)					
Resistance factor I ₉₀ 42.6					

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 104

COMPOUND NAME

OR NUMBER DOXYCYCLINE PARASITE (SUB)SPECIES *P. berghei*

FORMULATION *Tween 80/H₂O*... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3	5		-	67.1 ± 10.2
	1.0	5		-	47.8 ± 16.6
P	3.0	5	1	-	26.9 ± 10.4
	10.0	5		-	0.9 ± 0.9
	Ø	10		8.7	
ED ₅₀ (range) 0.8(0.2 - 2.1)					
ED ₉₀ (range) 3.2(0.8 - 8.0)					
Resistance factor I ₉₀ 1.2					
	0.3	5		-	100 ± 0.8
	1.0	5		-	96.9 ± 4.9
B	3.0	5	1	-	92.2 ± 2.3
	10.0	5		-	19.1 ± 8.2
	Ø	10		20.4	
ED ₅₀ (range) 6.1(3.1 - 10.8)					
ED ₉₀ (range) 17.5(9.0 - 30.0)					
Resistance factor I ₉₀ 6.5					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 105

COMPOUND NAME

DR NUMBER DOXYCYCLINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O.... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3	5		-	89.2 ± 3.5
	1.0	5		-	89.4 ± 5.9
PYR	3.0	5	1	-	43.2 ± 17.0
	10.0	5		-	10.0 ± 2.1
	Ø	10		23.1	
ED ₅₀ (range) 2.7(1.6 - 4.6)					
ED ₉₀ (range) 8.5(5.0 - 15)					
Resistance factor I ₉₀ 3.1					
	0.3	5		-	87.0 ± 11.5
	1.0	5		-	80.6 ± 7.4
ORA	3.0	5	1	-	74.2 ± 10.2
	10.0	5		-	38.4 ± 14.2
	Ø	10		13.7	
ED ₅₀ (range) 8.0(1.6 - 32.0)					
ED ₉₀ (range) 180(37.0 - 700)					
Resistance factor I ₉₀ 66.7					

Principal Investigator: Professor W.Peters
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TABLE 106

OR NUMBER Donycycline PARASITE (SUB) SPECIES P. berghei

FORMULATION Tween 80 / H₂O ROUTE OF ADMINISTRATION : SC / IP / PO / IV

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% $\times 100$
	0.3	5		-	96.7 \pm 1.9
	1.0	5		-	92.7 \pm 3.6
MEN	3.0	5	1	-	73.8 \pm 2.9
	10.0	5		-	22.0 \pm 5.0
	30.0	5		-	0.9 \pm 0.4
	ϕ	10			

ED₅₀(range) 4.2(3.0-6.0)

ED₉₀(range) 13.0(9.2-18.5)

Resistance factor I_{90} ED₅₀(range)ED₉₀ (range)Resistance factor I_{90}

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIOES)

TABLE 107

COMPOUND NAME

OR NUMBER DOXYCYCLINE PARASITE (SUB)SPECIES ... *P. berghei*

FORMULATION ... Tween 80 / H₂O ... ROUTE OF ADMINISTRATION : SC / IP / PO / IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.1	5		-	98.2 ± 2.1
	0.3	5		-	97.7 ± 3.1
NPN	1.0	5	1	-	71.7 ± 11.9
	3.0	5		-	48.6 ± 10.7
	10.0	5		-	9.5 ± 5.7
	Ø	10		11.1	

ED₅₀(range) 2.3 (1.3 - 4.0)

ED₉₀(range) 9.0 (5.0 - 15.5)

Resistance factor I₉₀ 3.3

	0.1	5		-	93.9 ± 3.4
	0.3	5		-	84.7 ± 7.7
N1708	1.0	5	1	-	87.6 ± 6.1
	3.0	5		-	86.9 ± 4.8
	10.0	5		-	75.7 ± 7.1
	Ø	10		20.6	

ED₅₀(range)

ED₉₀(range) > 10

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 108

COMPOUND NAME

OR NUMBER DOXYCYCLINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/HP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.1	5		-	100
	0.3	5		-	92.1 ± 9.7
MFY	1.0	5	1	-	56.3 ± 10.8
	3.0	5		-	57.2 ± 15.7
	10.0	5		-	64.5 ± 14.1
	∅	10		7.1	
ED ₅₀ (range)					
ED ₉₀ (range) > 10					
Resistance factor I ₉₀					
	0.1	5		-	84.3 ± 10.2
	0.3	5		-	72.3 ± 8.9
KFY	1.0	5	1	-	69.7 ± 10.3
	3.0	5		-	45.7 ± 7.7
	10.0	5		-	6.8 ± 2.7
	∅	10		13.0	
ED ₅₀ (range) 1.3(0.2 - 3.6)					
ED ₉₀ (range) 5.1(0.9 - 14.5)					
Resistance factor I ₉₀ 1.9					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIOES)

TABLE 109

COMPOUND NAME

OR NUMBER ... DOXYCYCLINE ... PARASITE (SUB)SPECIES ... *P. berghei* ...

FORMULATION ... Tween 80/H₂O ... ROUTE OF ADMINISTRATION : SC/TP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) ... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.1	5		-	97.8 ± 3.1
	0.3	5		-	93.5 ± 3.2
PFMA	1.0	5	1	-	85.0 ± 6.5
	3.0	5		-	76.0 ± 7.7
	10.0	5		-	30.5 ± 9.7
	∅	10		21.4	
ED ₅₀ (range) 6.3 (3.2 - 12.5)					
ED ₉₀ (range) 42.0 (21.0 - 85.0)					
Resistance factor I ₉₀ 15.6					
	0.1	5		-	89.0 ± 8.3
	0.3	5		-	91.7 ± 8.1
N 1765	1.0	5	1	-	97.0 ± 4.3
	3.0	5		-	51.8 ± 10.0
	10.0	5		-	21.6 ± 5.7
	∅	10		19.3	
ED ₅₀ (range) 4.0 (2.4 - 5.9)					
ED ₉₀ (range) 12.0 (7.3 - 18.0)					
Resistance factor I ₉₀ 4.4					

Principal Investigator: Professor W. Peters
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TABLE 110

OR NUMBER DOXYCYCLINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O... ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.1	5		-	100 ± 6.9
	0.3	5		-	100 ± 5.0
QM	1.0	5	1	-	100 ± 6.9
	3.0	5		-	75.7 ± 16.9
	10.0	5		-	60.5 ± 19.2
	∅	10		4.2	
ED₅₀(range) 8.0(3.5 - 17.0)					
ED₉₀(range) 18.0(8.0 - 40.0)					
Resistance factor I₉₀					
ED₅₀(range)					
ED₉₀(range)					
Resistance factor I₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE III

COMPOUND NAME

OR NUMBER ...DOXYCYCLINE..... PARASITE (SUB)SPECIES ...*P. yoelii*.....

FORMULATION ...Tween 80 / H₂O... ROUTE OF ADMINISTRATION : SC/IV/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.1	5		-	93.5 ± 4.3
	0.3	5		-	95.7 ± 3.3
NS	1.0	5	1	-	90.3 ± 3.0
	3.0	5		-	97.4 ± 3.0
	10.0	5		-	91.4 ± 4.2
	Ø	10		23.3	

ED₅₀(range)

ED₉₀(range) > 10

Resistance factor I₉₀

	0.1	5		-	88.9 ± 12.1
	0.3	5		-	77.8 ± 12.4
NS 1100	1.0	5	1	-	63.0 ± 12.8
	3.0	5		-	39.6 ± 6.4
	10.0	5		-	17.0 ± 2.8
	Ø	10		5.4	

ED₅₀(range) 1.7 (0.5 - 5.3)

ED₉₀(range) 28.0 (8.5 - 90.0)

Resistance factor I₉₀ 10.4

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 112

COMPOUND NAME

OR NUMBER ... DOXYCYCLINE ... PARASITE (SUB)SPECIES ... *P. yoelii* ...

FORMULATION ... Tween 80/H₂O ... ROUTE OF ADMINISTRATION : SC/1P/PO/IV

MAXIMUM TOLERATED DOSE (MTD) ... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.1	5		-	100
	0.3	5		-	93.0 ± 9.8
SH	1.0	5	1	-	98.2 ± 2.7
	3.0	5		-	95.4 ± 7.1
	10.0	5		-	37.2 ± 12.5
	∅	10		5.7	
ED ₅₀ (range) 8.0(6.2 - 10.0)					
ED ₉₀ (range) 17.0(13.5 - 21.5)					
Resistance factor I ₉₀ 6.3					
	0.1	5		-	100 ± 8.1
	0.3	5		-	89.7 ± 9.0
SPN	1.0	5	1	-	97.5 ± 7.2
	3.0	5		-	84.1 ± 7.5
	10.0	5		-	62.8 ± 14.7
	∅	10		6.4	
ED ₅₀ (range)					
ED ₉₀ (range) > 10					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 113

COMPOUND NAME

OR NUMBER ... DOXYCYCLINE ... PARASITE (SUB)SPECIES ... P. yepii

FORMULATION ... Tween 80 / H₂O ROUTE OF ADMINISTRATION : SC / IP / PO / IV

MAXIMUM TOLERATED DOSE (MTD) ... MG/KG X ...

Strain	Daily dose mg/kg 00-0+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x100
	0.1	5		-	100 ± 1.6
	0.3	5		-	100 ± 0.7
NS 1765	1.0	5	1	-	97.8 ± 1.4
	3.0	5		-	91.3 ± 4.4
	10.0	5		-	29.3 ± 9.0
	Ø	10		19.5	
EO ₅₀ (range) 6.8(5.5 - 8.5)					
EO ₉₀ (range) 15.5(12.5 - 19.0)					
Resistance factor I ₉₀ 5.7					
	0.1	5		-	80.7 ± 11.6
	0.3	5		-	88.6 ± 12.5
NS 1708	1.0	5	1	-	96.1 ± 4.4
	3.0	5		-	84.4 ± 7.2
	10.0	5		-	39.1 ± 7.4
	Ø	10		11.4	
EO ₅₀ (range) 8.0(4.7 - 14.5)					
EO ₉₀ (range) 34.0(20.0 - 62.0)					
Resistance factor I ₉₀ 12.6					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 114

COMPOUND NAME

OR NUMBER ... DOXYCYCLINE ... PARASITE (SUB)SPECIES ... *P. yoelii* ...

FORMULATION *Tween 80 / H₂O* ... ROUTE OF ADMINISTRATION : SC/IV/PO/IV

MAXIMUM TOLERATED DOSE (MTD) ... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	0.1	5		-	88.2 ± 8.8
	0.3	5		-	73.9 ± 15.3
QS	1.0	5	1	-	51.7 ± 4.6
	3.0	5		-	37.4 ± 3.3
	10.0	5		-	27.3 ± 3.6
	Ø	10		20.2	
ED ₅₀ (range) 1.5(0.8 - 2.8)					
ED ₉₀ (range) 32.0(20.0 - 72.0)					
Resistance factor I ₉₀ 11.9					
	0.1	5		-	71.9 ± 6.3
	0.3	5		-	83.8 ± 1.3
NIG	1.0	5	1	-	74.2 ± 8.1
	3.0	5		-	59.2 ± 9.8
	10.0	5		-	42.6 ± 8.7
	Ø	10		21.3	
ED ₅₀ (range)					
ED ₉₀ (range) >10					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 115

COMPOUND NAME

OR NUMBER ... DOXYCYCLINE ... PARASITE (SUB)SPECIES *P. yoelii* ...

FORMULATION ... Tween 80/H₂O ... ROUTE OF ADMINISTRATION : SC/IV/PO/IV

MAXIMUM TOLERATED DOSE (MTD) ... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.1	5		-	88.0 ± 14.8
	0.3	5		-	93.4 ± 2.3
SAM	1.0	5	1	-	89.6 ± 4.0
	3.0	5		-	71.1 ± 19.1
	10.0	5		-	43.6 ± 9.7
	∅	10		21.4	
ED ₅₀ (range) 7.2 (3.0 - 16.0)					
ED ₉₀ (range) 58.0 (24.0 - 125)					
Resistance factor I ₉₀ 21.5					
	0.1	5		-	84.5 ± 5.5
	0.3	5		-	85.9 ± 6.5
MPS	1.0	5	1	-	81.6 ± 12.7
	3.0	5		-	71.8 ± 12.0
	10.0	5		-	32.3 ± 8.5
	∅	10		8.8	
ED ₅₀ (range) 5.6 (2.8 - 14.5)					
ED ₉₀ (range) 42.0 (21.0 - 140)					
Resistance factor I ₉₀ 15.6					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 116

COMPOUND NAME

OR NUMBER ..DOXYCYCLINE..... PARASITE (SUB)SPECIES ...P. berghei....

FORMULATION Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3	5		-	100 ± 5.6
	1.0	5		-	69.1 ± 14.3
QMS	3.0	5	1	-	50.0 ± 18.8
	10.0	5		-	11.9 ± 5.6
	∅	10		8.6	
ED ₅₀ (range) 2.5(1.2 - 5.7)					
ED ₉₀ (range) 13.8(6.8 - 31.5)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 117

COMPOUND NAME **CM 6606**
OR NUMBER **...LON 1765**..... PARASITE (SUB)SPECIES **P. berghei**....
FORMULATION **Tween 80/H₂O** ROUTE OF ADMINISTRATION : **SC/IP/PO/IV**
MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	93.1 ± 5.0
	3.0	5		-	79.6 ± 7.4
NH	10.0	5	1	-	74.2 ± 9.3
	30.0	5		-	10.8 ± 5.2
	Ø	10		9.3	

ED₅₀(range) **8.8(3.7 - 30.0)**

ED₉₀(range) **39.0(16.0 - 130)**

Resistance factor I₉₀

ED₅₀(range)

ED₉₀(range)

Resistance factor I₉₀

Principal Investigator: Professor W. Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 118

COMPOUND NAME **CM 6606**

OR NUMBER **LON.1765**..... PARASITE (SUB)SPECIES **P. berghei**...

FORMULATION **Tween 80/H₂O** ROUTE OF ADMINISTRATION : **SC/IP/PO/IV**

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	100 ± 4.1
	3.0	5		-	30.0 ± 10.6
NS 1100	10.0	5	1	-	17.9 ± 6.5
	30.0	5		-	0
	Ø	10		5.6	
ED ₅₀ (range) 4.5(2.0 - 7.2)					
ED ₉₀ (range) 8.2(3.5 - 13.1)					
Resistance factor I ₉₀					
	1.0	5		-	92.6 ± 2.9
	3.0	5		-	70.5 ± 13.8
SAM	10.0	5	1	-	5.4 ± 1.4
	30.0	5		-	0.8 ± 0.4
	Ø	10		22.2	
ED ₅₀ (range) 3.5(2.1 - 7.1)					
ED ₉₀ (range) 10.6(6.2 - 22.0)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 119

COMPOUND NAME **CM 6606**

OR NUMBER **..LON.1765.....** PARASITE (SUB)SPECIES **..P.berghei...**

FORMULATION **Tween 80/H₂O** ROUTE OF ADMINISTRATION : **SC/10/10/10**

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	96.2 ± 9.6
	3.0	5		-	96.2 ± 10.9
QMS	10.0	5	1	-	72.4 ± 13.2
	30.0	5		-	34.8 ± 18.2
	Ø	10		5.8	
ED ₅₀ (range) 18.5(10.4 - 30.0)					
ED ₉₀ (range) 70.0(40.0 - 114)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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APPENDIX 3

SUMMARISED RESULTS OF DRUG INTERACTION STUDY
USING CHLOROQUINE AND VERAPAMIL.

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 120

COMPOUND NAME Verapamil
 DR NUMBER LON 2109..... PARASITE (SUB)SPECIES P. yoelii ssp.
 FORMULATION Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC/IP/PO/IV
 MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% _{X100}
	1.0	5		-	96.0
	3.0	5		-	94.9
NS	10.0	5	1	-	100
	30.0	5		-	97.6
	100.0	5 *		-	100
	Ø	10		23.2	
ED ₅₀ (range)		* ~ LD ₈₀ INACTIVE AT MTD			
ED ₉₀ (range)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
 Department of Medical Protozoology
 London School of Hygiene & Tropical Medicine

TABLE 121

OR NUMBER PARASITE (SUB)SPECIES *P. yopeli* ssp. ...

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 122

COMPOUND NAME

OR NUMBER *Verapamil + Chloroquine* PARASITE (SUB)SPECIES *P. yoelii ssp...*

FORMULATION *Tween 80 / H₂O* ROUTE OF ADMINISTRATION : *SC/IP/PO/IV*

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% X100
	1.0 + 0.3	5		-	94.4
	3.0 + 0.3	5		-	99.5
NS	10.0 + 0.3	5	1	-	96.3
	30.0 + 0.3	5		-	98.8
	100.0 + 0.3	5		-	>LD ₁₀₀
	Ø	10		23.2	
ED ₅₀ (range)		INACTIVE AT MTD			
ED ₉₀ (range)					
Resistance factor I ₉₀					
	1.0 + 1.0	5		-	100
	3.0 + 1.0	5		-	100
NS	10.0 + 1.0	5	1	-	87.9 ± 5.7
	30.0 + 1.0	5		-	96.4 ± 4.4
	100.0 + 1.0	5		-	>LD ₁₀₀
	Ø	10		23.2	
ED ₅₀ (range)		INACTIVE AT MTD			
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 123

COMPOUND NAME

OR NUMBER ...Verapamil + Chloroquine PARASITE (SUB)SPECIES ..*P. yoelii* ssp..

FORMULATION ..Tween 80/H₂O.. ROUTE OF ADMINISTRATION : SC/~~IP~~/~~PO~~/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x100
	1.0 + 3.0	5		-	34.9 ± 4.9
	3.0 + 3.0	5		-	26.2 ± 3.6
NS	10.0 + 3.0	5	1	-	13.2 ± 3.6
	30.0 + 3.0	5		-	10.9 ± 2.2
	100.0 + 3.0	5		-	> LD ₁₀₀
	∅	10		23.2	
ED ₅₀ (range) 8.2(3.2 - 28.0)					
ED ₉₀ (range) 13.5(5.2 - 45)					
Resistance factor I ₉₀					
	1.0 + 10.0	5		-	21.1 ± 7.0
	3.0 + 10.0	5		-	7.6 ± 3.4
NS	10.0 + 10.0	5	1	-	6.8 ± 1.6
	30.0 + 10.0	5		-	5.5 ± 2.5
	100.0 + 10.0	5		-	> LD ₁₀₀
	∅	10		23.2	
ED ₅₀ (range) 0.09(0.1 - 0.4)					
ED ₉₀ (range) 4.4(1.8 - 19.5)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 124

COMPOUND NAME

OR NUMBER Verapamil + Chloroquine. PARASITE (SUB)SPECIES *P. yoelii* ssp.

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0 + 30.0	5		-	11.4 ± 5.0
	3.0 + 30.0	5		-	5.6 ± 2.1
NS	10.0 + 30.0	5	1	-	4.0 ± 1.7
	30.0 + 30.0	5		-	4.9 ± 2.0
	100.0 + 30.0	5		-	> LD ₁₀₀
	Ø	10		23.2	
ED ₅₀ (range) 0.1 (0.1 - 0.8)					
ED ₉₀ (range) 3.0 (0.5 - 16.5)					
Resistance factor I ₉₀					
	1.0 + 60.0	5		-	5.2 ± 3.1
	3.0 + 60.0	5		-	4.0 ± 1.2
NS	10.0 + 60.0	5	1	-	2.8 ± 0.5
	30.0 + 60.0	5		-	1.0 ± 0.9
	100.0 + 60.0	5		-	> LD ₁₀₀
	Ø	10		23.2	
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 125

COMPOUND NAME

OR NUMBER *Chloroquine + Verapamil* PARASITE (SUB)SPECIES *P. yoelii* ssp....

FORMULATION *Tween 80 / H₂O* ROUTE OF ADMINISTRATION : SC/~~IP~~/~~PO~~/~~IV~~

MAXIMUM TOLERATED DDSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	0.3 + 1.0	5		-	94.4
	1.0 + 1.0	5		-	100
NS	3.0 + 1.0	5	1	-	34.9 ± 4.9
	10.0 + 1.0	5		-	21.1 ± 7.0
	30.0 + 1.0	5		-	11.4 ± 5.0
	60.0 + 1.0	5		-	5.2 ± 3.1
	∅	10		23.2	
ED ₅₀ (range) 8.0 (2.1 - 25.0)					
ED ₉₀ (range) 28.0 (4.6 - 55.0)					
Resistance factor I ₉₀					
	0.3 + 3.0	5		-	99.5
	1.0 + 3.0	5		-	100
NS	3.0 + 3.0	5	1	-	26.2 ± 3.6
	10.0 + 3.0	5		-	7.6 ± 3.4
	30.0 + 3.0	5		-	5.6 ± 2.1
	60.0 + 3.0	5		-	4.0 ± 1.2
	∅	10		23.2	
ED ₅₀ (range) 9.5 (1.8 - 25.0)					
ED ₉₀ (range) 21.0 (4.0 - 49.0)					
Resistance factor I ₉₀					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIOES)

TABLE 126

COMPOUND NAME

OR NUMBER *Chloroquine + Verapamil...* PARASITE (SUB)SPECIES *P. yoelii ssp...*

FORMULATION *Tween 80/H₂O...* ROUTE OF ADMINISTRATION : SC/ID/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% x 100
	0.3 + 10.0	5		-	96.3
	1.0 + 10.0	5		-	87.9 ± 5.7
NS	3.0 + 10.0	5	1	-	13.2 ± 3.6
	10.0 + 10.0	5		-	6.8 ± 1.6
	30.0 + 10.0	5		-	4.0 ± 1.7
	60.0 + 10.0	5		-	2.8 ± 0.5
	Ø	10		23.2	
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					
	0.3 + 30.0	5		-	98.8
	1.0 + 30.0	5		-	96.4 ± 4.4
NS	3.0 + 30.0	5	1	-	10.9 ± 2.2
	10.0 + 30.0	5		-	5.5 ± 2.5
	30.0 + 30.0	5		-	4.9 ± 2.0
	60.0 + 30.0	5		-	1.0 ± 0.9
	Ø	10		23.2	
ED ₅₀ (range) 3.4 (1.2 - 14.0)					
ED ₉₀ (range) 8.0 (2.7 - 34.0)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 127

COMPOUND NAME

OR NUMBER Verapamil PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0	5		-	100
	3.0	5		-	98.6
RC	10.0	5	1	-	100
	30.0	5		-	99.3
	∅	10		5.3	
ED ₅₀ (range)		INACTIVE AT MTD			
ED ₉₀ (range)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIDES)

TABLE 128

COMPOUND NAME

OR NUMBER

Chloroquine.....

PARASITE (SUB)SPECIES P. berghei....

FORMULATION Tween 80/H₂O. ROUTE OF ADMINISTRATION : SC/IV/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	3.0	5		-	99.8
	10.0	5		-	100
RC	30.0	5	1	-	100
	60.0	5		-	93.5 ± 4.6
	∅	10		5.3	
ED ₅₀ (range)		INACTIVE AT MTD			
ED ₉₀ (range)					
Resistance factor I ₉₀					
ED ₅₀ (range)					
ED ₉₀ (range)					
Resistance factor I ₉₀					

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SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTOCIOES)

TABLE 129

COMPOUND NAME

OR NUMBER Verapamil + Chloroquine PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H₂O ROUTE OF ADMINISTRATION : SC/10/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg 00-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0 + 3.0	5		-	100
	3.0 + 3.0	5		-	97.6 ± 3.1
RC	10.0 + 3.0	5	1	-	99.1 ± 2.5
	30.0 + 3.0	5		-	100
	∅	10		5.3	
EO ₅₀ (range)		INACTIVE AT MTD			
ED ₉₀ (range)					
Resistance factor I ₉₀					
	1.0 + 10.0	5		-	98.1 ± 1.1
	3.0 + 10.0	5		-	99.5 ± 0.3
RC	10.0 + 10.0	5	1	-	100 ± 2.0
	30.0 + 10.0	5		-	97.2 ± 1.6
	∅	10		5.3	
EO ₅₀ (range)		INACTIVE AT MTD			
EO ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS
(BLOOD SCHIZONTICIDES)

TABLE 130

COMPOUND NAME

DR NUMBER Verapamil + Chloroquine PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H₂O ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% Control PR% ^{x100}
	1.0 + 30.0	5		-	100
	3.0 + 30.0	5		-	100 ± 0.6
RC	10.0 + 30.0	5	1	-	96.3 ± 3.4
	30.0 + 30.0	5		-	98.1 ± 2.7
	∅	10		5.3	
ED ₅₀ (range)		INACTIVE AT MTD			
ED ₉₀ (range)					
Resistance factor I ₉₀					
	1.0 + 60.0	5		-	97.4 ± 3.9
	3.0 + 60.0	5		-	98.1 ± 2.4
RC	10.0 + 60.0	5	1	-	100
	30.0 + 60.0	5		-	96.3 ± 5.1
	∅	10		5.3	
ED ₅₀ (range)		INACTIVE AT MTD			
ED ₉₀ (range)					
Resistance factor I ₉₀					

Principal Investigator: Professor W. Peters
Department of Medical Protozoology
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APPENDIX 4

SUMMARY OF DATA FROM BLOOD SCHIZONTOCIDAL TESTS PERFORMED ON
WRAIR COMPOUNDS IN LIVERPOOL AND LONDON BETWEEN 1967 AND 1987.

SUMMARISED RESULTS OF BLOOD SCHIZONTOCIDAL ACTIVITY TESTS
PERFORMED ON WRAIR COMPOUNDS IN LIVERPOOL AND LONDON
BETWEEN 1967 AND 1987

EXPERIMENTAL MALARIA CHEMOTHERAPY UNIT
DEPARTMENT OF MEDICAL PROTOZOOLOGY
LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE
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PRINCIPAL INVESTIGATOR: PROFESSOR W. PETERS MD DSc

14 MAY 1987

INTRODUCTION

During the twenty year period between 1967 and 1987, the Principal Investigator has headed an experimental chemotherapy unit investigating candidate antimalarial compounds in a series of collaborative studies with the Walter Reed Army Institute of Research. These studies were commenced in the Department of Parasitology, Liverpool School of Tropical Medicine and transferred in 1980 to the Department of Medical Protozoology, London School of Hygiene and Tropical Medicine.

The data contained in this presentation have been prepared by re-examining the experimental data obtained over this period and recalculating the results by the techniques currently in use in order to provide a standardised series of Tables. This was necessary as our reporting procedures have changed over the twenty years of these collaborations.

The Tables show the ED₉₀ values and the Resistance Factor (I₉₀) for all the WRAIR compounds submitted for blood schizontocidal activity testing during this period, together with those obtained with a series of standard compounds and some primaquine analogues and metabolites which have been supplied from other American sources in connection with these studies.

MATERIALS AND METHODS

1. GENERAL CONDITIONS

Eperythrozoon coccoides free, random bred, male Swiss albino mice (TFW strain, supplied by A. Tuck and Son, Rayleigh, Essex) weighing between 18 and 20 grammes are used for all of the tests.

They are maintained in temperature controlled quarters

($22^{\circ} \pm 2^{\circ}\text{C}$) in batteries of plastic cages with five mice in each cage. The mice are fed Dixons No.86 diet and receive tap water ad libitum.

2. BLOOD SCHIZONTOCIDAL ACTIVITY

Evaluation of blood schizontocidal activity and cross resistance patterns is carried out by the employment of the "four day test" (Peters, 1970). A battery of fifteen strains of P.berghei, comprised of one drug sensitive strain (P.berghei KBG-173, "N strain") and fourteen lines resistant to a range of antimalarial drugs, is currently maintained for this purpose. Routinely, compounds are examined initially against the drug sensitive N strain and further studies utilising drug resistant lines are employed only when indicated, unless specifically requested.

PARASITE SPECIES AND STRAINS

All P.berghei or P.yoelii ssp.

- a. N (= Keyberg 173): Sensitive to all standard antimalarial drugs. Does not produce gametocytes. Maintained by syringe passage.
- b. NS (P.yoelii ssp.): Moderately resistant to chloroquine. Maintained by cyclical passage through Anopheles stephensi and syringe passage under drug pressure in mice (60 mg/kg s.c. once immediately following infection).
- c. RC - derived from N: Highly resistant to chloroquine. Maintained by syringe passage under drug pressure (60 mg/kg/day s.c.).

- d. P - derived from N: Highly resistant to primaquine. Maintained by syringe passage under drug pressure (60 mg/kg/day s.c.).
- e. B - derived from N: Highly resistant to cycloguanil hydrochloride. Maintained by syringe passage under drug pressure (60 mg/kg/day s.c.).
- f. PYR - derived from NK65: Highly resistant to pyrimethamine. Maintained by syringe passage under drug pressure (100 mg/kg i.p. once, following infection).
- g. ORA - derived from NK65: Highly resistant to sulphonamides. Maintained by syringe passage under drug pressure (1000 mg/kg sulphaphenazole s.c. once, following infection).
- h. N/1100 - derived from N: Highly resistant to mefloquine. Maintained by syringe passage under drug pressure (60 mg/kg s.c. once, following infection).
- i. MEN(N/1086) - derived from N: Highly resistant to menoctone. Maintained by syringe passage under drug pressure (60 mg/kg/day s.c.).
- j. NH - derived from N: resistant to halofantrine. Maintained by syringe passage under drug pressure (5.0 mg/kg s.c. once, following infection).
- k. NPN - derived from N: highly resistant to pyronaridine. Maintained by syringe passage under drug pressure (30 mg/kg s.c. once, following infection).
- l. Q - derived from N: highly resistant to quinine. Maintained by syringe passage under drug pressure (600 mg/kg p.o. once, following infection).
- m. ART - derived from NS: highly resistant to artemisinin. Maintained by syringe passage under drug pressure (150 mg/kg s.c. once, following infection).

n. N/1019 - derived from N: highly resistant to the Triazine WR 99210. Maintained by syringe passage under drug pressure (100 mg/kg s.c. once, following infection).

o. N/1708 - derived from N: highly resistant to the Mannich base WR 228258. Maintained by syringe passage under drug pressure (10 mg/kg s.c. once, following infection).

Blood Schizontocidal Test Protocol

Male, random-bred Swiss albino mice weighing 18 - 22 grammes are inoculated intravenously with 10^7 parasitised red blood cells of one of the above P.berghei strains. Animals are then dosed once daily for four consecutive days beginning on the day of infection. Compounds are dissolved or suspended in sterile distilled water with Tween 80 and administered subcutaneously, intraperitoneally or orally. Where exceptional difficulty is encountered in preparing an aqueous preparation, the test compound is first dissolved in dimethyl sulfoxide and, subsequently, aqueous dilutions are prepared for use. The parasitaemia is determined on the day following the last treatment and the ED₅₀ and ED₉₀, i.e. 50% and 90% suppression of parasites when compared with untreated controls, estimated from a plot of log dose : probit activity. Standard error is calculated with the aid of Table 48, Geigy Scientific Tables, 6th Edition. The degree of cross resistance is determined by comparing activity in the sensitive and resistant strains.

$$\text{Index of cross resistance} = \frac{\text{ED}_{50}/\text{ED}_{90} \text{ resistant line}}{\text{ED}_{50}/\text{ED}_{90} \text{ N strain}}$$

Notes

1. Peters, W. Drug resistance in Plasmodium berghei, Vincke and

Lips, 1948. I. Chloroquine resistance. Exp. Parasitol., 17, 89-90 (1965).

2. Peters, W., Portus, J.H. and Robinson, B.L. The chemotherapy of rodent malaria, XXII. The value of drug resistant strains of P. berghei in screening for blood schizontocidal activity. Ann. Trop. Med. Parasit., 69, 155-171, (1975).

PART ONE

STANDARD COMPOUNDS

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N1100	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
CHLOROQUINE DIPHOSPHATE	SC		3.1	56.0	18.1	230	742	2.3	0.7	4.8	1.5	3.5	1.1	3.6	1.2	4.5	1.5
AMODIAQUINE	SC		2.6	18.0	6.9	420	1615	2.0	0.8	2.1	0.8	3.3	1.3	2.6	1.0	20.0	7.7
PRIMAQUINE DIPHOSPHATE	SC		4.8	8.4	1.8	13.0	2.7	74.0	15.4	6.4	1.3	24.0	5.0	2.6	0.5	9.0	1.9
QUININE HYDROCHLORIDE	PO		118	290	2.5	2500	21.2	140	1.2	170	1.4	130	1.1	190	1.6	1700	14.4
CINCHONINE HYDROCHLORIDE	PO		125	220	1.8	3250	26.0	85.0	0.7	50.0	0.4	91.0	0.7	63.0	0.5	400	3.2
QUINIDINE HYDROCHLORIDE	PO		31.0	195	6.3	92.0	3.0	85.0	2.7	35.0	1.1	93.0	3.0	54.0	1.7	195	6.3
MEFLOQUINE	PO		4.6	7.2	1.6	275	598	13.5	2.9	6.0	1.3	5.6	1.2	4.2	0.9	540	117.4

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 1a

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	Q		NH		MEN		NPN		N1708		ART					
		ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
CHLOROQUINE DIPHOSPHATE	SC	>60	>19	7.0	2.3	3.0	1.0	25.0	8.1	10.2	3.3	>30	>97				
AMODIAQUINE HYDROCHLORIDE	SC	>30	>11.5	5.4	2.1	4.5	1.7	32.0	12.3	5.2	2.0	310	119.2				
PRIMAQUINE DIPHOSPHATE	SC	18.5	3.9	10.5	2.2	3.3	0.7	8.4	1.8	7.0	1.5	11.5	2.4				
QUININE HYDROCHLORIDE	PO	>600	>51	210	1.8	40.0	0.3	900	7.6	175	1.5	400	3.4				
CINCHONINE HYDROCHLORIDE	PO	>600	>4.8	290	2.3	60.0	0.5	550	4.4	90.0	0.7	700	5.6				
QUINIDINE HYDROCHLORIDE	PO	470	15.2	117	3.8			580	18.7	88.0	2.8	385	12.4				
MEFLOQUINE	PO	>60	13.0	9.0	2.0	2.5	0.5	6.8	1.5	5.3	1.2	65.0	14.1				

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 1 b

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N1100	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
HALOFANTRINE	SC		1.1	1.0	0.9	>30	>273	1.5	1.4	4.2	3.8	2.3	2.1	1.9	1.7	135	122.8
MEPACRINE	SC		1.9	18.3	9.6	17.0	8.9	2.9	1.5	4.6	2.4	1.1	0.6	2.1	1.1	195	102.6
ARTEMISININ	SC		4.2	10.0	2.4	630	150	12.0	2.9	8.2	2.0	4.8	1.1	7.5	1.8	17.0	4.0
PYRONARIDINE	SC		0.7	1.2	1.7	10.0	14.3	1.0	1.4	1.4	2.0	1.1	1.6	1.5	2.1	1.6	2.3
CYCLOQUANIL HYDROCHLORIDE	SC		3.3	6.9	2.1	3.6	1.1	>10	>3.0	>100	>30.3	>100	>30.3	44.0	13.3	2.5	0.8
PYRIMETHAMINE	iP		0.12	0.11	0.9	0.05	0.4	0.17	1.4	2.4	20.0	3.4	28.3	0.5	4.2	0.04	0.3
SULFADOXINE	SC		4.4	0.26	0.06	0.62	0.14	0.39	0.09	0.71	0.16	1.9	0.4	29.0	6.6	0.04	0.01

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 2a

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	Q		NH		MEN		NPN		N1708		ART			
		ED	I	ED	I	ED	I	ED	I	ED	I	ED	I	ED	I
HALOFANTRINE	SC	>100	>91	3.6	3.3	0.7	0.6	3.5	3.2	1.5	1.4	6.5	5.9		
MEPACRINE	SC	>30	>5.8	4.7	2.5			45.0	23.7	12.3	6.5	>30	>5.8		
ARTEMISININ	SC	>30	>7.1	10.5	2.5	6.2	1.5	90.0	21.4	5.9	1.4	16.5	39.3		
PYRONARIDINE	SC	>100	>143	0.8	1.1	0.7	1.0	13.5	19.3	0.7	1.0	19.5	27.9		
CYCLOQUANIL HYDROCHLORIDE	SC	3.4	1.0	6.4	1.9	5.2	1.6	10.0	3.0	3.7	1.1	6.3	1.9		
PRIMETHAMINE	ip	0.03	0.25	0.26	2.2	0.4	3.3	0.21	1.8	0.01	0.08	0.05	0.4		
SULFADOXINE	SC	0.13	0.03	2.7	0.6	0.34	0.08	0.1	0.02	1.2	0.3	0.05	0.01		

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

Table 2b

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N1100	
		ED	50	ED	90	I	ED	90	I	ED	90	ED	90	ED	90	ED	90
PYRIMETHAMINE + SULFADOXINE (1:3)	ip			0.32	0.1	0.3	0.06	0.19	0.2	0.6	0.52	1.6	3.0	9.4	0.48	1.5	0.08 0.3
MENOCTONE	sc			1.4	4.5	3.2	11.0	7.9	2.1	1.5	9.0	6.4	7.2	5.1	2.7	1.9	1.2 0.9
FLOXACRINE	sc			1.0	0.6	0.6	0.3	0.3	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.3 0.3
CLINDAMYCIN	sc			36.0	56.0	1.5	56.0	1.6	6.4	0.2	27.0	0.8	6.0	0.2	8.8	0.2	2.9 0.1
DOXYCYCLINE	sc			2.7	>10	>3.7	3.8	1.4	3.2	1.2	17.5	6.5	8.5	3.1	180	66.7	33.0 12.2
	sc																
	sc																

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 3 a

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	Q		NH		MEN		NPN		N1708		ART					
		ED	I	ED	I	ED	I	ED	I	ED	I	ED	I	ED	I	ED	I
PYRIMETHAMINE + SULFADOXINE (1:3)	ip	0.01	0.03	0.16	0.5	0.07	0.2	0.03	0.1	0.1	0.3	0.05	0.16				
MENOCTONE	sc	1.8	1.3	1.6	1.1	30	21.4	1.8	1.3	2.3	1.6	1.2	0.9				
FLOXACRINE	sc	0.5	0.5	0.8	0.8	1.0	1.0	0.3	0.3	0.6	0.6	0.3	0.3				
CLINDAMYCIN	sc	9.7	0.3	57.0	1.6	7.5	0.2	9.0	0.3	27.0	0.8	10.0	0.3				
DOXYCYCLINE	sc	9.3	3.4	20.0	7.4			9.0	3.3	21.0	13.7	32.0	11.9				
	sc																
	sc																

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 3b

PART TWO

WRAIR COMPOUNDS

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		F/R		ORA		N 1019	
		ED	50	ED	90	I	ED	90	I	ED	90	ED	90	ED	90	ED	90
WR 27653 RC 12 Naphthalene disulfonate	sc																
WR 3102 3-piperonyl sydnone	sc	100	340	135	0.4	118	0.3	325	1.0	145	0.4	100		90.0	0.3		
WR 5949 Trimethoprim lactate	sc	23.5	190					105	0.6	290	1.5			340	1.8		
WR 6010 Metachloridine	sc	3.0	24.0					6.1	0.25					115	4.8		
WR 99210	sc	0.3	0.6	1.6	2.7	0.6	1.0	0.7	1.2	1.1	1.8	0.4	0.7	0.3	0.5	5.1	8.5
	po	1.4	2.7			0.6	0.2			1.1	0.4						
WR 3090 B	sc	5.0	18.3	5.8	0.4	107	6.7	74.0	4.0	37.0	2.0	800	43.7	69.0	3.8		
WR 5677 B AE 06841	sc	12.0	38.0			250	6.6	35.0	0.9	14.3	0.4	120	3.2	>100	>2.6		

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 4

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA			
		ED ₅₀	ED ₉₀	ED ₅₀	ED ₉₀	ED ₅₀	ED ₉₀	ED ₅₀	ED ₉₀	ED ₅₀	ED ₉₀	ED ₅₀	ED ₉₀	ED ₅₀	ED ₉₀	ED ₅₀	ED ₉₀
WR 49808	sc	0.7	3.2			11.0	3.4	2.1	0.7	9.0	2.8	7.2	2.3	2.7	0.8		
WR 6798 H difomyl dapstone	sc	0.2	0.4	0.4	1.0	0.9	2.3	5.7	14.3	9.8	24.5	0.3	0.75	4.5	11.3		
WR 9838 - B-O ZC 23620	sc	9.0	33.0			28.0	0.8	23.5	0.7	32.5	1.0	19.0	0.6	40.0	1.2		
WR 33063 AD	sc	13.0	88.0			~9000	~102	60.0	0.7	>300	>3.4	160	1.8				
WR 40070 AD AF 10617	sc	100	245	200	0.8	235	1.0	280	1.1	>500	>2.1	380	1.6	580	2.4		
WR 5949 AE AF 87431	sc	12.0	105			160	1.5	>300	>3.0	>300	>3.0	>300	>3.0				
WR 118176 AA AC 87355	sc	1.1	1.7	2.8	1.6	>100	>590	1.8	1.1	1.2	0.7	1.8	1.1	1.2	0.7		

TABLE 5

* Interpolated graphically

MTD = maximum tolerated dose

ED₅₀ / ED₉₀ = mg/kg x 4

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N1086	
		ED	ED 50	ED	ED 90	I	ED	ED 90	I	ED	ED 90	ED	ED 90	ED	ED 90	ED	ED 90
WR 99662 AB AT 88428	SC	18.0	40.0				110	2.8	22.0	0.6	23.0	0.7	18.0	0.5			
WR 157835 AW 23379	SC	1.1	10.0	13.0	1.3		>100	>10.0	>30	7.0	7.0	21.5	2.2	1.4	0.1		
WR 157830	SC	11.5	46.0	69.0	1.5		46.0	1.0	51.0	1.1	55.0	1.2	43.0	0.9	21.5	0.5	
WR 54036 AB AF 92799	SC		>1000	>300			~1500										
WR 148703 AE AX 28619	SC	5.3	7.6														
	PO	48.0	74.0														
WR 161085 AB AX 26820	SC	2.6	4.5				2.5	0.6	47.0	10.4	19.0	4.2	4.4	1.0	3.1	0.7	
WR 5994 AJ AX 44276	SC		>300														

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 6

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N 1086	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
WR 6012 AG AV 96493	SC	0.6	1.5	2.1	1.4	2.5	1.7	2.1	1.4	1.6	1.1	2.4	1.6	2.3	1.5		
	PO	0.8	2.1														
WR 33063 AE AV 34854	SC	9.5	33.2			~4900	~148	34.8	1.0								
WR 49808 Menectone	SC	0.7	1.5	4.5	3.0	11.0	7.3	2.1	1.4	9.0	6.0	7.2	4.8	2.7	1.8	>100	>66.7
	PO	1.1	3.5														
WR 131836 AE AX 64080 1,2,4 acetylated menectone	SC	52.0	94.0			56.0	1.1	74.0	1.4	90.0	1.7						
	PO	56.0	130														
WR 30090 AH AU 34863	SC	3.4	5.5	9.7	1.8	3000	545	2.8	0.5	7.6	1.4	1.1	0.2	1.8	0.3		
	PO	0.9	1.5	3.0	2.0	560	373	1.6	1.1	1.9	1.3						
WR 113618 AT 88437	SC	1.1	1.9	2.7	1.4	3.6	1.9	0.8	0.4	1.7	0.9	1.4	0.7	1.5	0.8		
	PO	1.2	3.4														
WR 135403 AX 26982	SC	0.2	0.5			0.5	1.0	0.8	1.6	3.2	6.4	0.6	1.2	3.6	7.2		
	PO	0.1	0.3			0.4	1.3	1.0	3.3	3.3	11.0	0.5	1.7				

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 7a

[illegible]
$$\text{ED}_{50} / \text{ED}_{90} = \text{mg/kg} \times 4 \quad \text{MTD} = \text{maximum tolerated dose}$$

TABLE 7b

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N1100	
		ED	50	ED	90	I	ED	90	I	ED	90	ED	90	ED	90	ED	I
WR 142490 AX 23187 Mefloquine	SC	1.5	4.6	7.2	1.6	275	59.8	13.5	2.9	6.0	1.3	5.6	1.2	4.2	0.9	540	118
	PO	3.4	5.2														
WR 142490 AE AY 65742 Mefloquine	SC	1.5	3.0	10.0	2.7	>1000	>450										
		1.0	2.2														
WR 166391 AA AX 61481 †	SC	~225	>1000														
	PO	~172	~460														
WR 166391 AA †	SC	14.5	39.0	>100	>2.6	>100	>2.6										
	PO	145	790														
WR 122455 AG	SC	4.1	9.9	19.0	1.9	280	28.3	14.3	1.4	12.6	1.3	30.0	3.0	14.5	1.5	730	3.0
	PO	3.3	7.0	11.5	1.6	380	54.3	6.0	0.9	6.4	0.9						
WR 164861 AA AX 57772	SC	1.4	6.2	163	26.3	>1000	161	54.0	8.7	780	126	323	52.1	78.0	12.6		
	PO	2.9	5.5														
WR 36971 AB AF 55385	SC	775	2300														
	PO	825	8500														

ED₅₀ / ED₉₀ = mg/kg x 4

MTD = maximum tolerated dose

† No consistent results obtained

TABLE 8a

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	Q		NH		MEN		NPN		ART							
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
WR 142490 AX 23187 Mefloquine	SC	>60	>13	9.0	2.0	2.5	0.5	6.8	1.5	65.0	14.1						

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose Table 8 b

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA	
		ED	ED	ED	I	ED	I	ED	I	ED	I	ED	I	ED	I
		50	90	90	90	90	90	90	90	90	90	90	90	90	90
WR 91808 AB AS 52352	sc	6.1	14.3	11.0	0.8	97.0	6.8	6.7	0.5	11.3	0.8	14.5	1.0	5.2	0.4
	po	5.4	15.4												
WR 99682 AB AT 70453	sc	12.0	37.0	48.0	1.3	400	10.8	20.5	0.6	40.0	1.1	105	2.8	23.0	0.6
	po	12.9	24.7												
WR 99662 AB AT 88428	sc	30.8	50.2	41.0	0.8	1000	19.9	37.3	0.7	33.0	0.7	34.0	0.7	20.0	0.4
	po	30.9	54.0												
WR 90558 AC AV 21316	sc	3.2	7.2	6.4	0.9	11.2	1.6	2.5	0.3	6.3	0.9	3.1	0.4	25.0	3.5
	po	3.6	11.3												
WR 137812 AV 45432	sc	1.0	2.1	3.4	1.6	5.4	2.6	5.6	2.7	52.0	24.8	84.0	40.0	11.5	5.5
	po	0.6	1.6												
WR 77135 AB ZC 86529	sc	19.0	163	440	2.7	>1000	>6.1	>300	>1.8	460	2.8	680	4.2	825	5.1
	po	19.3	178												
WR 171870 A AX 65381	sc	83.0	140	153	1.1										
	po	22.0	37.5	40.0	1.1										

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 9

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
WR 150762 AB AX 64044	sc	1.1	2.8	2.7	1.0	35.5	12.7	1.9	0.7	2.1	0.8	2.4	0.9	2.3	0.8
	po	0.9	1.8	1.7	0.9										
WR 176990 A AY 63168	sc	2.4	16.4	8.3	0.5										
	po	13.8	28.5	20.5	0.7										
WR 177602 AB AY 93362	sc	1.3	5.0	4.0	0.8										
	po	3.0	4.3	4.3	1.0										
WR 169355 AA AX 63696	sc		300												
	po		300												
WR 165355 AB AX 76062	sc	1.1	2.6	3.8	1.5										
	po	1.7	3.0	2.8	0.9										
WR 8684 SN 10960	sc	9.0	25.1	19.0	0.8										
	po	5.8	13.3	21.0	1.6										
WR 106147 AD AY 97897	sc	2.0	4.6	10.1	2.2	7.3	1.6	46.5	10.1						
	po	5.0	10.0	19.4	1.9										

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 10

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N 1100	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
WR 187046 AA BB 43932 Cycloquine	SC	0.3	0.5	3.7	7.4	52.0	104	0.7	1.4	0.5	1.0	0.6	1.2	0.7	1.4		
WR 7573-B-9 AJ 32261	SC	34.0	70.0	110	1.6	>1000	14.3										
WR 104361 AC BC 23775	SC	0.1	0.2	0.6	3.0	0.7	3.5	0.6	3.0	0.5	2.5	0.6	3.0	0.4	2.0		
WR 159251 AA AW 91877	SC	9.0	265	460	1.7											200	0.8
WR 6025 AO AG 75480, BE21431	PO	4.7	215	300	1.4											150	0.7
WR 6025 AO AG 75480, BE21431	SC	15.5	30.0														
WR 6026 A-1 AG 75499	SC	0.6	1.6			5.5	3.4	7.3	4.6								
WR 187177 AA BB 44064	SC	60.0	800														

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 11

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA	
		ED	50	ED	90	I	ED	90	I	ED	90	I	ED	90	I
WR 172 688 AB BB 48419	SC		160	600											
WR 7312 A-1 BB 47761	SC		75.0	170											
WR 179305 AD BB 47734	SC		11.0	15.5						>100	>6.5	>100	>6.5		
WR 184520 AA BB 41670	SC		41.0	175											
WR 113254 AB BB 48455	SC		115	>300											
WR 189294 BE 46719	SC		4.0	11.0			4.8	0.4	>100	>9.1	20.0	1.8			
WR 159248 AA AW 91840	SC		39.0	>100	>100										

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 12

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA	
		ED	ED 50	ED	I 90	ED	I 90	ED	I 90	ED	I 90	ED	I 90	ED	I 90
WR 93133 AC BB 59636	SC	9.0	>100	>100		>100		>100		>100		>100		>100	
WR 196469 AA BC 51797	SC	11.5	50.0												
WR 3102 - B-0 ZB 69309	SC	15.8	52.0												
3-piperonyl sydnone WR 199782 AA BC 99948	PO	20.0	150												
	SC	>100	>100												
	PO	>30	>30												
WR 197236 AA BC 71128	SC	1.0	2.4												
WR 199509 AA BC 60036	SC	>100	>100												
	SC	>30	>30												
WR 190830 AB BD 29165	SC	18.2	36.5	39.0	1.1	105	2.9								

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 13

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N			NS			RC			P			B			PYR			ORA			N 1086		
		ED	50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90			
WR 4931 - B-0 ZB 38055	SC	46.0	>MTD	>MTD	>MTD																				
WR 118 176 AB BD 29941	SC	41.0	>100																						
WR 159 817 AA AX 20597	SC	55.0	133																						
WR 93156 AA AB 65238	SC	>300	>300																						
WR 152520 AB BC 52936 S-fluoro-oxalic acid	SC	0.2	1.0	5.2	5.2	5.2	3.8	3.8	3.8	5.1	5.1	3.1	3.1	1.9	1.9	2.5	2.5	1.7	1.7						
WR 126187 AC BD 41233	SC	>100	>100	>100	>100																				
WR 182232 AC BE 08456	SC	3.2	7.3																						
	PO	4.2	7.8																						

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 14

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	N			NS			RC			P			B			PYR			ORA		
		ED	50	ED	ED	90	I	ED	ED	90	I	ED	ED	90	I	ED	ED	90	I	ED	ED	90
WR 213640 AA BE 09999	SC	13.8	27.0	143	5.3	35.0	1.3	360	13.3													
WR 210809 AB BE 18292	SC	>100	>100																			
WR 194343 AA BC 06452	SC	1.5	4.2																			
	PO	3.9	7.6																			
WR 215295 AA BE 16378	SC	4.6	11.0																			
	PO	5.6	11.7																			
WR 216100 AA BE 17491	SC	2.1	5.6																			
	PO	2.6	6.1																			
WR 226296 AA BG 44452	SC	0.4	1.0	1.9	1.9	0.6	0.6	26.0	26.0													
	PO	0.2	0.5	2.9	5.8	0.7	1.4	7.8	15.6													
WR 220594 AA BE 84652	SC	>30	>30																			

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 15

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N 1100	
		ED	50	ED	90	ED	90	ED	90	ED	90	ED	90	ED	90	ED	90
WR 220 679 AA BE 96303	sc	>30	>30														
WR 219130 AA BE 58643	sc	2.5	4.7														
	po	6.5	12.5														
WR 228769 AA BG 66403	sc	>30	>30														
	po	>30	>30														
WR 229046 AA BG 67179	sc	>30	>30														
	po	>30	>30														
WR 194965 AD BG 33940	sc	2.0	3.5														
	po	1.2	1.7														
WR 225449 AA ZN 43971	sc	2.0	3.3	13.0	3.9	>30	>9.1									8.1	2.5
	po	1.8	2.4	2.7	1.1	>30	>12.5										
WR 129577 AC AW 41662	sc	23.5	155														
	po	<30	>30														

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 16

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N1100	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
WR 225448 BG 37402	sc	0.2	0.3	0.8	2.7	0.4	1.3	1.2	4.0							0.4	1.3
	po	0.1	0.2	0.6	3.0	0.6	3.0	1.2	6.0								
WR 25979-E-1 AH 78744 Nitroguanil	sc	29.0	45.0														
	sc	0.5	0.9													6.9	7.7
WR 99210 AE AW 23628	sc		<1.0														
	po	7.6	19.0														
WR 194965 AG BG 56327	sc	2.0	3.9	3.3	0.8	>60	>154										
	po	1.4	2.8	3.1	1.1	>10	>3.6										
WR 225449 AB BG 94925	sc	0.7	1.2													9.0	7.5
WR 232584 AA BH 05361	sc	0.3	0.5	1.9	3.8	0.4	0.8	2.1	4.2								
	po	0.4	0.6	3.2	5.3	0.9	1.5	2.6	4.3								

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 17

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N 1026	
		ED	ED 50	ED	I 90	ED	I 90	ED	I 90	ED	I 90	ED	I 90	ED	I 90	ED	I 90
WR 232143 AA BH 01069	sc	16.5	50.0														
WR 232956 AA BH 08773	sc	0.2	0.4	1.2	2.9	1.1	2.7	3.7	9.0	0.4	1.1	0.2	0.4	0.3	0.6		
	po	0.3	0.5	1.7	3.8	1.0	2.1	2.3	5.0	0.5	1.1	0.2	0.5	0.2	0.4		
WR 233078 AA BH 08764	sc	0.03	0.11	0.6	5.5	0.6	5.5	1.2	11.0	0.4	3.6	0.2	1.8	<0.3	<3.0		
	po	0.03	0.14	1.0	7.1	1.0	7.1	2.8	20.0	0.6	4.3	0.2	1.4	0.2	1.4		
WR 233195 AA BH 10086	sc	0.1	0.4	1.3	3.3	0.8	2.0	3.2	8.0	0.7	1.8	0.5	1.3	0.5	1.3		
	po	0.2	0.5	1.5	3.0	0.9	1.8	4.0	8.0	0.7	1.4	0.4	0.8	0.5	1.0		
WR 235485 AA BH 35570	sc	0.6	1.7	2.4	1.4	2.5	1.5	65.0	39.4							1.2	0.6
	po	0.7	2.5	2.3	0.9	1.5	0.6	11.0	4.4								
WR 212293 AB BH 49943	sc	12.0	126														
	po	30.0	270														
WR 233637 AB BH 49596	sc	15.0	29.0														
	po	1.8	4.5														

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 18a

[illegible]
$$\text{ED}_{50} / \text{ED}_{90} = \text{mg/kg} \times 4 \quad \text{MTD} = \text{maximum tolerated dose}$$

TABLE 18b

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N 1100	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
WR 237222 BH 57098	sc	1.8	3.1									3.4	1.1				
	ip	1.7	3.4									3.6	1.1				
WR 194965 AG BG 56327	sc	2.2	3.8	4.2	1.1	MTD											
WR 228258 AH BJ 30663	sc	4.0	10.0	2.9	0.3	13.0	1.3									26.0	2.6
	po	1.2	2.4													18.0	7.9
WR 225448 AG BH 58522	sc	0.2	0.3	0.4	0.8	0.4	1.3	1.2	4.0							0.4	1.3
	po	0.1	0.2	0.6	3.0	0.6	3.0	1.2	6.0								
WR 142490 AS BH 10371 Mefloquine HCl	sc	1.2	4.6	7.2	1.6	275	59.8	13.5	2.9	6.0	1.3	5.6	1.2	4.2	0.9	540	117
WR 2975 AW BJ 08241 Primquine diphosphate	sc	2.1	4.8	8.4	1.8	13.0	2.7	74.0	15.4	6.4	1.3	24.0	5.0	2.6	0.5	9.0	1.9
WR 2977 AV AG 64870 Anodiaquine	sc	1.1	2.6	18.0	6.9	420	162	2.0	0.8	2.1	0.8	3.3	1.3	2.6	1.0	20.0	7.7

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 19 a

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

TABLE 19b
$$ED_{01} / ED_{05} = \text{mg/kg} \times 4 \quad \text{MTD} = \text{maximum tolerated dose}$$

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N 1100	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
WR 1544 BN AG 64978 Chloroquine diphosphate	SC	1.6	3.1	56.0	18.1	230	74.2	2.3	0.7	4.8	1.5	3.5	1.1	3.6	1.2	4.5	1.5
WR 61112 AB 65541 Clodolol	SC	81.0	163	128	0.8											148	0.9
WR 158124 BD 22997	SC	13.5	42.0														
WR 44450 AD AY 29540	SC	0.6	1.6														
WR 102796 AD BC 78878	SC	1.7	4.2														
WR 194343 ZN 41968	SC	7.4	82.0														
WR 245082 BK 02771	SC	3.0	45.1	18.4	0.4											24.0	0.5

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 20 a

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

[illegible]

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 20b

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N 1100	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
WR 246976 BK 02780	SC	7.0	39.0	15.0	0.4											20.5	0.5
WR 250016 BK 16140	SC	3.5	12.2														
WR 6865 BK 23850 AQD	SC	200	>MTD	>MTD	-											>MTD	-
WR 15081 AY 15653 MAQ	SC	52.0	>MTD	>MTD	I 90 17.5 0.1											ED 50 13.0	I 90 0.1
WR 6890 BK 12713 AQL	SC	20.0	>300	>30	I 90 37.0 0.7											ED 50 29.0	I 90 0.6
WR 249684 AB BK 51550	SC	>300	>300													>30	
WR 250548 AA BK 51621	SC	5.1	36.0														

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 21

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N1100	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
WR 250547 AA BK 51630	SC	1.3	3.5														
WR 199508 AD BK 56500	SC	3.8	10.4														
WR 64306 Ph 4007	SC	42.0	170														
WR 64315 Ph 4017	SC	39.0	112														
WR 64324 Ph 4900	SC	53.0	153														
WR 64333 Ph 4901	SC	26.0	78.0														
WR 203659 ZN 39913 Clindamycin	SC	6.4	36.0	55.0	1.5	56.0	1.6	6.4	0.2	27.0	0.8	6.0	0.2	8.8	0.2	2.9	0.1

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 22a

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

[illegible]
$$\text{ED}_{50} / \text{ED}_{90} = \text{mg/kg} \times 4 \quad \text{MTD} = \text{maximum tolerated dose}$$

TABLE 22b

SUMMARY OF BLOOD SCHIZOTROPICIDAL (4 DA: TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N 1100	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
WR 251855 AA BK 71178	SC	0.3	0.7														
WR 171669 AD BB 43807 Halofenrine	SC	0.6	1.1	1.0	0.9	>30	27.3	1.5	1.4	4.2	3.8	2.3	2.1	1.9	1.7	135	123
WR BK 74491	SC	0.6	3.4														
WR BK 73127	SC	0.5	2.1														
WR 254594 BL 07762	SC	10.0	600														
WR BL 09686	SC	31.0	80.0														
WR BK 45678 Safromycin A	SC	>MTD	>MTD														

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 23a

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

[illegible]

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose

TABLE 23b

PART THREE

PRIMAQUINE ANALOGUES AND METABOLITES FROM OTHER SOURCES

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90
RKP 94 ¹	SC	>MTD	>MTD												
LON 1803															
1	SC	7.4	23.5												
LON 1804															
RKP 102 ¹	SC	>30	>30												
LON 1805															
RKP 100 ¹	SC	7.0	18.0												
LON 1806															
RCCJM 52 ¹	SC	2.0	5.0												
5-methoxyprimaquine															
LON 1807															
RCCJM 55 ¹	SC	4.0	10.5												
5,6-dihydroxy derivative of 5-hydroxyprimaquine															
LON 1808															
RKP 101 ¹	SC	6.8	22.5												
Mannich base derivative of primaquine															
LON 1809															

TABLE 24

¹ McChesney

MTD = maximum tolerated dose

ED₅₀ / ED₉₀ = mg/kg x 4

SUMMARY OF BLOOD SCHIZONTICIDAL (4 DAY TEST) DATA

	Route	N		NS		RC		P		B		PYR		ORA		N 1100	
		ED	50	ED	90	I	ED	90	I	ED	90	I	ED	90	I	ED	90
RCJM 53 ¹ 5-hydroxyprimaquine LON 1810	SC		3.8	6.0													
RCJM 97 ¹ 3-bromo primaquine LON 1908	SC		2.4	5.7													
N-ethoxycetyl primaquine ² LON 1920	SC		>100	>100	>100											>100	
SD4 HPQ ³ LON 1967	SC		23.0	330													
	SC																
	SC																
	SC																

ED₅₀ / ED₉₀ = mg/kg x 4 MTD = maximum tolerated dose 1 Mc Chesney 2 Bröss 3 Stroher TABLE 25

APPENDIX 5

SUMMARY OF CAUSAL PROPHYLACTIC TESTS PERFORMED ON WRAR COMPOUNDS
IN LIVERPOOL AND LONDON BETWEEN 1967 AND 1987.

SUMMARISED RESULTS OF CAUSAL PROPHYLACTIC ACTIVITY TESTS
PERFORMED ON WRAIR COMPOUNDS IN LIVERPOOL AND LONDON
BETWEEN 1967 AND 1987

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21 JULY 1987

INTRODUCTION

During the Principal Investigator's collaboration with WRAIR in Liverpool and London, a large number of putative antimalarials have been examined for causal prophylactic activity. Definitive results from these tests are given in the tables below. Where it has not been possible to reach the Minimum Fully Effective Dose because of toxicity or lack of compound, results are expressed as being more than either the Maximum Tolerated Dose or the highest dose tested as appropriate.

As would be expected, the test protocol has evolved to some extent over the years but no essential changes have occurred which prevent a valid retrospective comparison being made. The current test protocols are given below.

2. GENERAL CONDITIONS

Eperythrozoon coccoides free, random bred, male Swiss albino mice (TFW strain, supplied by A.Tuck and Son, Rayleigh, Essex) weighing between 18 and 20 grammes are used for all of the tests.

They are maintained in temperature controlled quarters ($22^{\circ} \pm 2^{\circ}\text{C}$) in batteries of plastic cages with five mice in each cage. The mice are fed Dixons No.86 diet and receive tap water ad libitum.

3. CAUSAL PROPHYLACTIC ACTIVITY

For the routine examination of compounds for causal prophylactic activity, we use the modified form of the technique described by Gregory and Peters (1970) and later elaborated by Peters et al (1975). In spite of the inherent disadvantage of

being unable to differentiate between direct action on the hepatic schizont and an effect on the emerging blood stages in the presence of both causal prophylactic and marked residual activity by this technique, we feel that for the majority of compounds this has proved to be the most satisfactory of the tests available, other than the use of P.cynomolgi in the rhesus monkey with its intrinsic problems. In this context, it should also be stressed that unlike the rhesus monkey/P.cynomolgi system, the rodent model is designed to demonstrate causal prophylactic action and not antirelapse activity.

PARASITE SPECIES

P.yoelii nigeriensis(N67;NIG): A moderate level of resistance to chloroquine is an inherent characteristic of this strain, which has never been exposed to any type of drug pressure. Maintained by cyclical transmission through A.stephensi (Lahore strain) without drug pressure.

Causal Prophylactic Test Protocols

(a) Preliminary prophylactic screening test

This test is designed to indicate the presence of any form of prophylactic activity in mice infected with P.y.nigeriensis.

Three groups of TFW mice (3 mice/group) are used for each compound in this test.

Group 1 Sporozoite inoculum at D+0.

Group 2 Sporozoite inoculum at D+0; 30 mg/kg s.c. test compound two hours post infection.

Group 3 Sporozoite inoculum at D+0; 100 mg/kg s.c. test compound two hours post infection.

The sporozoite inoculum is prepared from A. stephensi fed 10 - 14 days earlier on infected TFW mice. The mosquitoes are stunned by concussion and homogenised by hand in a Teflon grinder with Locke's solution with added 5 % w/v bovine serum albumin (Fraction V). The suspension is lightly centrifuged, decanted and 0.2 ml inocula of the supernatant are given intravenously to mice. Approximately 300 mosquitoes are used to infect 50 mice.

Compounds are dissolved or suspended in sterile distilled water with Tween 80 and administered subcutaneously, intraperitoneally or orally. Where exceptional difficulty is encountered in preparing an aqueous preparation, the test compound is first dissolved in dimethyl sulfoxide and, subsequently, aqueous dilutions are prepared for use. Unless an alternative route is indicated, the compounds are routinely administered subcutaneously.

The dose levels used have been arbitrarily selected to give an indication of the doses to be used in the full causal prophylactic test, and may be varied when necessary, e.g. where the test compound is toxic at the proposed dose.

Stained blood films from each animal are examined at D+7 and D+14. The results are expressed only as positive or negative and four categories of activity are recognised.

Grade 1	? Fully active.....	0/3 positive
Grade 2	? Active.....	1/3 positive
Grade 3	? Slightly active.....	2/3 positive
Grade 4	Inactive.....	3/3 positive

This preliminary screen affords a simple method of determining the presence or absence of activity and also, by extension of the dose range, it enables a large number of compounds to be screened rapidly to determine the probable

effective dose prior to examination in the more time consuming full causal prophylactic test.

(b) Causal prophylactic test

This test is designed to differentiate between prophylactic activity and residual suppressive effect of test compounds in rodent malaria infections. It does not indicate the presence of antirelapse activity since there is no comparable stage in this infection to the hypnozoite of P.cynomolgi or P.vivax.

The test is based on the inverse linear relationship between the logarithm of the sporozoite inoculum and the mean time taken for the resulting erythrocytic infection rate in groups of mice to reach 2 per cent. This relationship is valid only in an established range and breaks down if

- (i) the sporozoite inoculum is insufficient to give 100 per cent patency, or
- (ii) the sporozoite inoculum is extremely large.

Further, the test depends on the finding that

- (a) the minimum prepatent period is between 47 and 50 hours (48 hours has been assigned for purposes of calculation)
- and (b) the growth rate and drug sensitivity of the erythrocytic stage of the parasite is independent of the source, i.e. whether derived from injected sporozoites or parasitised red blood cells (RBC).

The original test contained a control group which received infected RBC only as well as the control which was infected with both sporozoites and RBC, but a statistical analysis of several hundred control animals has shown that there is no significant difference in the mean prepatent period between these groups.

Therefore the control receiving only RBC has been dropped from the test and , as a result ,the calculation of residual and prophylactic activity has become much simpler.

Four groups of mice are used in the test:

Group 1 Sporozoite inoculum on D0; saline at D0+2 hours.

Group 2 Sporozoite inoculum on D0; test compound at D0+2 hours.

Group 3 As Group 1 + RBC at D0+48 hours.

Group 4 As Group 2 + RBC at D0+48 hours.

The sporozoite inoculum is prepared and administered as described for the preliminary screening technique.

The blood inoculum, from infected TFW strain mice, is given intravenously in a volume of 0.2 ml and contains 10^7 infected RBC in isotonic saline. The parasite used is the N67(NIG) strain of P.y.nigeriensis.

Test compounds are prepared and administered in the manner described for the preliminary test.

Daily blood films are made and examined from D+3 until the parasitaemia reaches 2 per cent. Any animals which do not show patent infection by D+14 are considered to be negative.

Differences in the pre-2 per cent patency period (P2PP) between control and treated sporozoite inoculated animals can reflect a drug action on EE stages, erythrocytic forms or both. Cross-inoculation in parallel series of groups with infected RBC allows the residual drug action on erythrocytic forms to be assessed, leaving a value proportional to the effect on the EE stages only.

Hence, if P2PP Group 1 = a, P2PP Group 2 = b
and P2PP Group 3 = c, P2PP Group 4 = d

Then, (b-a) = Total activity
 (d-c) = Residual activity
 (b-a) - (d-c) = Causal prophylactic activity

Where negative values or positive values less than 0.5 are obtained from these calculations they should be regarded as zero.

References

1. Gregory, K.G. and Peters, W. The chemotherapy of rodent malaria, IX. Causal prophylaxis, Part 1. A method for demonstrating drug action on erythrocytic stages. Ann.Trop.Med. Parasit., 64, 15-24,(1970).
2. Peters, W., Davies, E.E. and Robinson, B.L. The chemotherapy of rodent malaria, XXIII. Causal prophylaxis, Part 2. Practical experience with Plasmodium yoelii nigeriensis in drug screening. Ann.Trop.Med.Parasit., 69, 311-328,(1975).

WR NUMBER	BN	MFED	RESIDUAL ACTIVITY(D+2)
WR 3102	-	30 - 100	NIL AT 300
WR 5949	-	600 - 1000	NIL AT 1000
WR 6010	-	30 - 100	NIL AT 100
WR 99210	-	1 - 3	NIL AT 3
WR 27653	-	INACTIVE AT 300	
WR 3090 B	-	> 10	MARKED AT 10
WR 5677 B	AE 06841	10 - 30	NIL AT 100
WR 6798 H	-	> 1	PRESENT AT 1
WR 9838 B-O	ZC 23620	30 - 100	NIL AT 100
WR 40070 AD	AF 10617	30 - 100	NIL AT 100
WR 118176 AA	AC 87355	30 - 50	NIL AT 50
WR 157835	AW 23379	> 300	NIL AT 300
WR 157830	-	INACTIVE AT MTD (30)	
WR 148703 AE	AX 28619	10 - 30	NIL AT 30
WR 161085 AB	AX 26820	INACTIVE AT MTD (100)	
WR 5994 AJ	AX 47276	> 1000	NIL AT 1000
WR 6012 AG	AV 96493	10 - 30	NIL AT 30
WR 49808	-	3 - 10	NIL AT 10
WR 131836	AX 64080	100 - 300	NIL AT 300
WR 30090 AH	AU 34863	300 - 1000	NIL AT 1000
WR 113618	AT 88437	> 100	PRESENT AT 100
WR 135403	AX 26982	0.1 - 0.3	PRESENT AT 3.0
WR 142490	AX 23187	30 - 100	MARKED AT 30
WR 166391 AA	AX 61481	> 300 po	NIL AT 300
WR 122455 AG	AX 76053	> 60	MARKED AT 60
WR 164861 AA	AX 57772	INACTIVE AT 30	MARKED AT 100
WR 36971 AB	AF 55385	INACTIVE AT 300	
WR 91808 AB	AS 52352	3 - 10	MARKED AT 100

WR NUMBER	BN	MFED	RESIDUAL ACTIVITY(D+2)
WR 99682 AB	AT 70453	30 - 100	PRESENT AT 100
WR 90558 AC	AV 21316	10 - 30	PRESENT AT 30
WR 137812	AV 45432	1 - 3	NIL AT 3
WR 77135 AB	ZC 86529	30 - 100	PRESENT AT 30
WR 106147 AD	AY 97897	10 - 30	NIL AT 30
WR 27351 AO	ZM 77810		INACTIVE AT MTD (300)
WR 104361 AC	BC 23775	10 - 30	NIL AT 30
WR 159251 AA	AW 91877	10 - 30	NIL AT 30
WR 6025 A-O	AG 75480		INACTIVE AT MTD (300)
WR 6026 A-I	AG 75499		INACTIVE AT MTD (100)
WR 187177 AA	BB 44064		INACTIVE AT MTD (100)
WR 172688 AB	BB 48419		INACTIVE AT 300
WR 7312 A-I	BB 47761		INACTIVE AT 300
WR 179305 AD	BB 47734	3 - 10	NIL AT 30
WR 184520 AA	BB 41670		INACTIVE AT MTD (100)
WR 113254 AB	BB 48455		INACTIVE AT 300
WR 189294	BE 46719	30 - 100	NIL AT 100
WR 44450 CO	AY 29540	1 - 3	MARKED AT 10
WR 188303 AA	BB 45543		INACTIVE AT 1000
WR 182058	AY 98947	1 - 3	NIL AT 30
WR 159248 AA	AW 91840	> 300	NIL AT 300
WR 93133 AC	BB 59636		INACTIVE AT 300
WR 3102 B-O	ZB 69309	30 - 100	NIL AT 100
WR 199782 AA	BC 99948	> 100 (MTD)	NIL AT 100
WR 197236 AA	BC 71128	1 - 3	MARKED AT 3
WR 199509 AA	BC 60036	100 - 300	NIL AT 300
WR 203736 AA	BD 53796		INACTIVE AT 1000
WR 190830 AB	BD 29165	30 - 100	NIL AT 100

WR NUMBER	BN	MFED	RESIDUAL ACTIVITY(D+2)
WR 4931 B-O	ZB 38055	30 - 100	NIL AT 100
WR 202437 AA	BD 26164	10 - 30	NIL AT 30
WR 49577 AE	BD 27698	> 30 (MTD)	NIL AT 30
WR 181721 AB	BD 27161	INACTIVE AT 1000	
WR 118176 AB	BD 29941	INACTIVE AT MTD (100)	
WR 199507 AB	BD 24062	INACTIVE AT MTD (10)	
WR 206027 AA	BD 54471	> 100 (MTD)	NIL AT 100
WR 200669 AA	BD 24213	> 750 (MTD)	NIL AT 750
WR 29634 AB	BD 04622	30 - 100	NIL AT 100
WR 159817 AA	AX 20597	30 - 100	NIL AT 100
WR 93156 AA	AB 65238	> 1000	NIL AT 1000
WR 205439 AA	BD 54195	1 - 3	NIL AT 3
WR 183489 AD	BD 56671	INACTIVE AT 1000	
WR 189296 AA	BB 46595	INACTIVE AT MTD (300)	
WR 5990 AA	AG 99266	INACTIVE AT MTD (10)	
WR 181023 AE	BD 57427	30 - 100	NIL AT 100
WR 207878 AA	BD 57481	INACTIVE AT 1000	
WR 207717 AA	BD 57258	> 1000	MARKED AT 1000
WR 152520 AB	BC 52936	> 1000	PRESENT AT 1000
WR 206281 AA	BD 54776	INACTIVE AT 300	
WR 179443 AC	BD 57436	INACTIVE AT MTD (300)	
WR 183489 AE	BD 57552	INACTIVE AT 300	
WR 208177 AA	BD 57712	INACTIVE AT 1000	
WR 182230 AB	BD 58040	> 1000	NIL AT 1000
WR 203607 AA	BD 27652	30 - 100	NIL AT 100
WR 203608 AA	BD 27661	1 - 3	NIL AT 10
WR 210441 AA	BE 10849	> MTD (10)	NIL AT MTD
WR 210447 AA	BE 10965	INACTIVE AT MTD (300)	

WR NUMBER	BN	MFED	RESIDUAL ACTIVITY(D+2)
WR 210446 AA	BE 10983	INACTIVE AT MTD (300)	
WR 210434 AA	BE 11024	INACTIVE AT MTD (300)	
WR 182234 AA	BE 10198	3 - 10	NIL AT 10
WR 210551 AA	BE 11588	> 100	TRACE AT 100
WR 210550 AA	BE 11597	30 - 100	NIL AT 100
WR 210809 AA	BE 11275	> 1000	NIL AT 1000
WR 603259 AC	BE 10429	10 - 30	NIL AT 100
WR 126187 AC	BD 41223	INACTIVE AT 300	
WR 208442 AA	ED 57981	30 - 100	NIL AT 300
WR 211815 AA	BE 08527	30 - 100	PRESENT AT 30
WR 181517 AB	BE 12370	30 - 100	NIL AT 300
WR 211532 AA	BE 12567	100 - 300	MARKED AT 300
WR 212577 AA	BE 13493	> 300 (MTD)	NIL AT 300
WR 182232 AC	BE 08456	100 - 300	PRESENT AT 100
WR 213640 AA	BE 09999	> 300 (MTD)	NIL AT 300
WR 211814 AB	BE 12905	0.1 - 0.3	NIL AT 30
WR 214703 AA	BE 15040	100 - 300	NIL AT 300
WR 214706 AA	BE 15077	100 - 300	PRESENT AT 100
WR 215296 AA	BE 16369	10 - 30	NIL AT 30
WR 182234 AD	BE 17580	3 - 10	NIL AT 30
WR 214403 AA	BE 14776	INACTIVE AT 300	
WR 210809 AB	BE 18292	> 1000	TRACE AT 1000
WR 158122	-	1 - 3	NIL AT 3
WR 201678 AB	BE 13304	10 - 30	NIL AT 30
WR 211674 AB	BE 20587	INACTIVE AT MTD (300)	
WR 211816 AA	BE 20630	30 - 60	NIL AT 60
WR 215295 AA	BE 16378	> 300	MARKED AT 300
WR 29594 AC	BE 20014	10 - 30	NIL AT 30

WR NUMBER	BN	MFED	RESIDUAL ACTIVITY(D+2)
WR 218336 AA	BE 66832	> MTD (100)	NIL AT 100
WR 218335 AA	BE 66930	10 - 30	NIL AT 30
WR 199385 AB	BE 19575	10 - 30	NIL AT 30
WR 194343 AA	BC 06452	60 - 100	NIL AT 100
WR 219382 AA	BE 71226	30 - 60	NIL AT 60
WR 219783 AA	BE 75948	INACTIVE AT 600	
WR 219784 AA	BE 75939	60 - 100	NIL AT 300
WR 218670 AB	BE 59088	> 100 (MTD)	PRESENT AT 100
WR 216893 AA	BE 19477	> 600 (MTD)	NIL AT 600
WR 2975 E-19	AG 64745	30 - 60	NIL AT 60
WR 6027 A-O	AG 75828	30 - 60	NIL AT 60
WR 127854 AC	BE 20087	30 - 60	NIL AT 60
WR 181023 AG	BE 50003	10 - 30	NIL AT 30
WR 6020 AD	BE 20783	> 60	NIL AT 60
WR 6020 AC	BE 21066	60 - 100 po	NIL AT 100
WR 6021 AK	BE 20907	125 - 150 po	NIL AT 150
WR 5990 AD	AG 99266	30 - 60 po	NIL AT 60
WR 161085 AB	AX 26820	30 - 60	NIL AT 60
WR 211814 AB	BE 12905	1 - 3	NIL AT 10
WR 212624 AA	BE 13822	30 - 60	MARKED AT 100
WR 215295 AA	BE 16378	100 - 300	MARKED AT 300
WR 216100 AA	BE 17491	> 100	MARKED AT 100
WR 217124 AA	BE 43759	30 - 60	NIL AT 60
WR 218676 AA	BE 55820	10 - 30	NIL AT 30
WR 152149 AB	BE 66770	> 100 (MTD)	NIL AT 100
WR 217154 AA	BE 67204	30 - 60	NIL AT 60
WR 219874 AA	BE 79802	1 - 3	NIL AT 30
WR 222671 AA	BG 11891	30 - 60	NIL AT 100

WR NUMBER	BN	MFED	RESIDUAL ACTIVITY(D+2)
WR 222890 AA	BG 13831	> 300	TRACE AT 300
WR 211533 AC	BG 38034	> 150 (MTD)	NIL AT 150
WR 226296 AA	BG 44452	1 - 3	NIL AT 10
WR 215761 AA	BE 16967	10 - 30	NIL AT 30
WR 226426 AA	BG 45208	1 - 3	NIL AT 3
WR 226626 AA	BG 46714	1 - 3	NIL AT 10
WR 199361 AC	BG 47168	1 - 3	NIL AT 3
WR 206891 AB	BG 47462	30 - 60	MARKED AT 60
WR 216693 AB	BG 47239	INACTIVE AT 100	
WR 227495 AA	BG 56738	> 30 (MTD)	NIL AT 30
WR 227681 AA	BG 56612	60 - 100	MARKED AT 100
WR 228000 AA	BG 58367	10 - 30	NIL AT 30
WR 227988 AA	BG 58447	INACTIVE AT 300	
WR 228002 AA	BG 58189	1 - 3	NIL AT 10
WR 228327 AA	BG 60698	60 - 100	NIL AT 100
WR 228335 AA	BG 60689	10 - 30	NIL AT 30
WR 220594 AA	BE 84652	INACTIVE AT 100	
WR 220679 AA	BE 96303	10 - 30	NIL AT 30
WR 219130 AA	BE 58643	10 - 30	NIL AT 30
WR 226937 AA	BG 55008	30 - 60	NIL AT 30
WR 226762 AA	BG 47293	INACTIVE AT 100	
WR 226899 AA	BG 52623	1 - 3	NIL AT 10
WR 225374 AA	BG 37591	INACTIVE AT MTD (30)	
WR 228457 AA	BG 62790	30 - 60	NIL AT 60
WR 228456 AA	BG 62807	1 - 3	NIL AT 3
WR 228583 AA	BG 63644	10 - 30	NIL AT 30
WR 228769 AA	BG 66403	INACTIVE AT 100	
WR 228710 AA	BG 66412	1 - 3	NIL AT 10

WR NUMBER	BN	MFED	RESIDUAL ACTIVITY(D+2)
WR 228708 AA	BG 66798	10 - 30	NIL AT 30
WR 229046 AA	BG 67179	INACTIVE AT 100	
WR 229011 AA	BG 67099	> 100	NIL AT 100
WR 229092 AA	BG 68354	INACTIVE AT 100	
WR 229238 AA	BG 70112	INACTIVE AT 100	
WR 194965 AD	BG 33940	10 - 30	NIL AT 60
WR 225449 AA	ZN 43971	10 - 30	MARKED AT 10
WR 226292 AA	BG 44541	3 - 10	NIL AT 10
WR 211666 AB	BG 11417	10 - 30	NIL AT 30
WR 212579 AB	BG 48969	60 - 100	NIL AT 100
WR 226257 AA	BG 44425	30 - 100	NIL AT 100
WR 129577 AC	AW 41662	INACTIVE AT 100	
WR 225448	BG 37402	10 - 30	MARKED AT 10
WR 221527	BG 48898	1 - 3	NIL AT 30
WR 229431	BG 70578	INACTIVE AT 100	
WR 229397	BG 70596	INACTIVE AT 100	
WR 229406	BG 70603	INACTIVE AT 100	
WR 229396	BG 70630	INACTIVE AT 100	
WR 229398	BG 70658	INACTIVE AT 100	
WR 215733	ZN 43328	INACTIVE AT 100	
WR 212223	ZN 43391	30 - 100	NIL AT 100
WR 218804	ZN 43426	3 - 10	NIL AT 10
WR 224097	ZN 43953	> 100	NIL AT 100
WR 229429	BG 70667	INACTIVE AT 100	
WR 229427	BG 70550	INACTIVE AT 100	
WR 4396 AR	BG 66421	INACTIVE AT MTD (30)	
WR 206513 AB	BG 79017	INACTIVE AT 100	
WR 230388 AA	BG 81580	INACTIVE AT 100	

WR NUMBER	BN	MFED	RESIDUAL ACTIVITY(D+2)
WR 230395 AA	BG 81599	INACTIVE AT 100	
WR 230394 AA	BG 81606	INACTIVE AT 100	
WR 230387 AA	BG 81615	10 - 30	NIL AT 30
WR 230386 AA	BG 81624	INACTIVE AT 100	
WR 230216 AA	BG 80967	INACTIVE AT 100	
WR 230212 AA	BG 80994	INACTIVE AT 100	
WR 230225 AA	BG 81035	INACTIVE AT 100	
WR 230284 AA	BG 81222	INACTIVE AT 100 (MTD)	
WR 206287 AB	BG 81759	INACTIVE AT 100	
WR 230621 AA	BG 83191	INACTIVE AT 100	
WR 222119 AB	BG 81740	INACTIVE AT 100	
WR 1544 BM	AR 20613	INACTIVE AT 100	
WR 184806 AH	ZN 37115	> 30	NIL AT 30
WR 33063 AF	AW 43746	INACTIVE AT 30	
WR 171669 AE	BB 43914	10 - 30	NIL AT 30
WR 172435 AC	AY 98670	10 - 30	NIL AT 30
WR 180409 AC	BE 99420	> 30	NIL AT 30
WR 448 AG	AG 22874	10 - 30	NIL AT 30
WR 6798 AL	AF 50013	3 - 10	NIL AT 10
WR 93133 AC	BB 59627	10 - 30	NIL AT 30
WR 179305 AD	BB 47734	> 30	-
WR 38839 B	AM 33272	1 - 3	NIL AT 3
WR 99210 AE	AW 23628	1 - 3	NIL AT 30
WR 14871 AB	AX 26848	0.3 - 1	TRACE AT 1
WR 159412 AC	BB 59823	0.1 - 0.3 po	NIL AT 3 po
WR 159412 AC	BB 59823	1 - 3	NIL AT 3
WR 180872 AC	BD 09556	< 3	NIL AT 3
WR 81844 AD	ZF 92291	> 30	NIL AT 30

WR NUMBER	BN	MFED	RESIDUAL ACTIVITY(D+2)
WR 87781 AB	AB 34313	INACTIVE AT 30	
WR 231030 AA	BG 89077	10 - 30	MARKED AT 30
WR 231033 AA	BG 89086	10 - 30	MARKED AT 30
WR 231138 AA	BG 89362	30 - 100	NIL AT 100
WR 230837 AA	BG 85408	INACTIVE AT 30	
WR 231350 AA	BG 94630	INACTIVE AT 30	
WR 231633 AA	BG 94907	INACTIVE AT 30	
WR 231530 AA	BG 94916	30 - 60	NIL AT 60
WR 232584 AA	BH 05361	10 - 30	NIL AT 30
WR 232143 AA	BH 01069	3 - 10	NIL AT 10
WR 218573 AA	BE 66994	INACTIVE AT 30	
WR 232956 AA	BH 08773	30 - 100	NIL AT 100
WR 233078 AA	BH 08764	10 - 30	TRACE AT 30
WR 233195 AA	BH 10086	10 - 30	TRACE AT 30
WR 7295 AD	BB 49961	INACTIVE AT 30	
WR 181613 AB	BG 62110	INACTIVE AT 30	
WR 3863 B-O	AG 75775	> 30	MARKED AT 30
WR 61112 AC	AF 10895	INACTIVE AT 30	
WR 219423 AA	BE 73480	3 - 10	NIL AT 30
WR 96345 AB	BC 64589	3 - 10	PRESENT AT 10
WR 194905 AB	BG 00754	1 - 3	NIL AT 3
WR 233627 AA	BH 13989	10 - 30	NIL AT 30
WR 150017 AC	BH 30097	3 - 10	NIL AT 30
WR 155004 AC	BH 30104	1 - 3	PRESENT AT 3
WR 233821 AA	BH 16711	10 - 30	NIL AT 30
WR 235485 AA	BH 35570	30 - 100	PRESENT AT 100
WR 235780	BH 37514	INACTIVE AT 30	
WR 235781	BH 37532	INACTIVE AT 30	

WR NUMBER	BN	MFED	RESIDUAL ACTIVITY(D+2)
WR 212293 AB	BH 49943	3 - 10	NIL AT 30
WR 233637 AB	BH 49596	INACTIVE AT 30	
WR 237230	BH 57016	INACTIVE AT 30	
WR 237233	BH 57025	INACTIVE AT 30	
WR 237234	BH 57043	INACTIVE AT 30	
WR 237227	BH 57052	INACTIVE AT 30	
WR 237222	BH 57098	> 30	NIL AT 30
WR 237264	BH 57392	INACTIVE AT 30	
WR 156949	AV 99850	INACTIVE AT 30	
WR 236066	BH 39634	INACTIVE AT 30	
WR 234749 AB	BH 67503	INACTIVE AT 30	
WR 228258 AH	BJ 30663	10 - 30	NIL AT 30
WR 9792	AJ 63248	3 - 10	NIL AT 30
WR 158124	BD 22997	10 - 30	NIL AT 30
WR 238605	BH 69990	10 - 30	NIL AT 30
WR 243789	BJ 08189	10 - 30	NIL AT 30
WR 246315	BJ 45691	1 - 3	NIL AT 30
WR 237375	BH 58120	INACTIVE AT 30	
WR 242511 AA	BH 89438	1 - 3	NIL AT 30
WR 242511 AB	BJ 78592	1 - 3	NIL AT 30
WR 44450 AD	AY 29540	3 - 10	PRESENT AT 3
WR 102796 AD	BC 78878	1 - 3	NIL AT 30
WR 194343	ZN 41968	> 30	NIL AT 30
WR 245082	BK 02771	10 - 30	TRACE AT 10
WR 246796	BK 02780	> 30	NIL AT 30
WR 250016	BK 16140	INACTIVE AT 30	
WR 6865	BK 23850	10 - 30	TRACE AT 30
WR 15081	BK 12713	10 - 30	NIL AT 30

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